=> file reg
FILE 'REGISTRY' ENTERED AT 11:39:47 ON 16 JUL 2008

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DICTIONARY FILE UPDATES: 15 JUL 2008 HIGHEST RN 1034171-01-1

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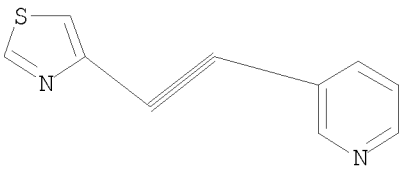
http://www.cas.org/support/stngen/stndoc/properties.html

=> d que
L1 STR



Structure attributes must be viewed using STN Express query preparation.
L3 222 SEA FILE=REGISTRY SSS FUL L1
L4 66 SEA FILE=CAPLUS L3

=> d l4 1-66 ibib abs hitstr
YOU HAVE REQUESTED DATA FROM FILE 'CAPLUS' - CONTINUE? (Y)/N:y

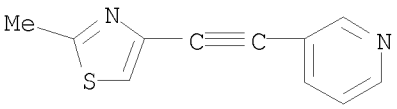
L4 ANSWER 1 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:442890 CAPLUS
DOCUMENT NUMBER: 148:577071
TITLE: Transcriptional profiling of the rat frontal cortex following administration of the mGlu5 receptor antagonists MPEP and MTEP
AUTHOR(S): Gass, Justin T.; Olive, M. Foster
CORPORATE SOURCE: Center for Drug and Alcohol Programs, Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, SC, 29425, USA
SOURCE: European Journal of Pharmacology (2008), 584(2-3), 253-262

CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The development of selective type 5 metabotropic glutamate receptor (mGlu5) antagonists, such as 2-methyl-6-(phenylethynyl)-pyridine (MPEP) and 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]-pyridine (MTEP), has revealed an important role for these receptors in various disorders of the nervous system including depression, anxiety, epilepsy, Parkinson's disease, drug addiction, and alcoholism. In this study, we used microarray technol. to examine changes in gene expression induced by repeated administration of the mGlu5 antagonists MPEP and MTEP. Male Wistar rats (n = 5 per treatment group) were administered MPEP (10 mg/kg), MTEP (10 mg/kg) or vehicle i.p. twice daily for 5 days. Approx. 30 min following the final drug administration, rats were sacrificed and frontal cortices were then dissected and examined for changes in gene expression by cDNA microarray anal. Changes in gene expression with p-values less than 0.01 were considered to be statistically significant. The expression of 63 genes was changed by both MPEP and MTEP, with 58 genes down-regulated and 5 genes up-regulated. Quant. PCR verified the magnitude and direction of change in expression of 9 of these genes (r 2 = 0.556, p = 0.017). Pathway anal. revealed that many of the biol. processes altered by repeated MPEP and MTEP treatment were related to ATP synthesis, hydrolase activity, and signaling pathways associated with mitogen-activated protein kinase (MAPK). Our results demonstrate diverse effects of MPEP and MTEP gene expression in the frontal cortex, and these results may help elucidate the mechanisms by which these compds. produce beneficial effects in animal models of various disorders of the central nervous system.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transcriptional profiling of rat frontal cortex following administration of mGlu5 receptor antagonists MPEP and MTEP)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:181354 CAPLUS
DOCUMENT NUMBER: 148:304660
TITLE: Mood disorders: Regulation by metabotropic glutamate receptors
AUTHOR(S): Pilc, Andrzej; Chaki, Shigeyuki; Nowak, Gabriel; Witkin, Jeffrey M.
CORPORATE SOURCE: Institute of Pharmacology, Polish Academy of Sciences and Collegium Medicum, Jagiellonian University, Krakow, Pol.
SOURCE: Biochemical Pharmacology (2008), 75(5), 997-1006
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review

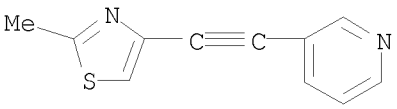
LANGUAGE: English

AB A review. Medicinal therapies for mood disorders neither fully serve the efficacy needs of patients nor are they free of side-effect issues. Although monoamine-based therapies are the primary current treatment approaches, both preclin. and clin. findings have implicated the excitatory neurotransmitter glutamate in the pathogenesis of major depressive disorders. The present commentary focuses on the metabotropic glutamate receptors and their relationship to mood disorders. Metabotropic glutamate (mGlu) receptors regulate glutamate transmission by altering the release of neurotransmitter and/or modulating the post-synaptic responses to glutamate. Convergent biochem., pharmacol., behavioral, and clin. data will be reviewed that establish glutamatergic neurotransmission via mGlu receptors as a biol. relevant process in the regulation of mood and that these receptors may serve as novel targets for the discovery of small mol. modulators with unique antidepressant properties. Specifically, compds. that antagonize mGlu2, mGlu3, and/or mGlu5 receptors (e.g. LY341495, MGS0039, MPEP, MTEP) exhibit biochem. effects indicative of antidepressant effects as well as in vivo activity in animal models predictive of antidepressant efficacy. Both preclin. and clin. data have previously been presented to define NMDA and AMPA receptors as important targets for the modulation of major depression. In the present review, we present a model suggesting how the interplay of glutamate at the mGlu and at the ionotropic AMPA and NMDA receptors might account for the antidepressant-like effects of glutamatergic- and monoaminergic-based drugs affecting mood in patients. The current data lead to the hypothesis that mGlu-based compds. and conventional antidepressants impact a network of interactive effects that converge upon a down regulation of NMDA receptor function and an enhancement in AMPA receptor signaling.

IT 329205-68-7, MTEP
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mood disorders regulation by metabotropic glutamate receptors)

RN 329205-68-7 CAPLUS

CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 97 THERE ARE 97 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:146165 CAPLUS

DOCUMENT NUMBER: 148:440819

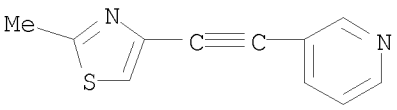
TITLE: Antidepressant-like actions of minocycline combined with several glutamate antagonists

AUTHOR(S): Molina-Hernandez, Miguel; Tellez-Alcantara, Norma Patricia; Perez-Garcia, Julian; Olivera-Lopez, Jorge Ivan; Jaramillo-Jaimes, M. Teresa

CORPORATE SOURCE: Laboratorio de Conducta, Instituto de Investigaciones Psicologicas, Universidad Veracruzana, Jalapa, Veracruz, 91000, Mex.

SOURCE: Progress in Neuro-Psychopharmacology & Biological Psychiatry (2008), 32(2), 380-386
CODEN: PNPPD7; ISSN: 0278-5846

PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study tested the potential antidepressant activity of minocycline alone or combined with two traditional antidepressant drugs or several glutamate receptor antagonists, using the time sampling method in the forced swimming test. Results showed that: desipramine (10.0 mg/kg, P < 0.05; 15.0 mg/kg, P < 0.05), minocycline (60.0 mg/kg, P < 0.05; 80.0 mg/kg, P < 0.05) and EMQMCM (1.5 mg/kg, P < 0.05; 2.0 mg/kg, P < 0.05), reduced immobility by increasing climbing. Fluoxetine (20.0 mg/kg, P < 0.05; 25.0 mg/kg, P < 0.05) reduced immobility by increasing swimming. MTEP (5.0 mg/kg, P < 0.05; 10.0 mg/kg, P < 0.05) and dizolcipine (1.0 mg/kg, P < 0.05; 1.5 mg/kg, P < 0.05) reduced immobility by increasing swimming and climbing. Combination expts. showed that a subthreshold dose of minocycline (50.0 mg/kg) synergized the antidepressant-like actions of subthreshold doses of: desipramine (5.0 mg/kg; P < 0.05), EMQMCM (0.6 mg/kg; P < 0.05), MTEP (2.5 mg/kg; P < 0.05) and dizolcipine (0.5 mg/kg; P < 0.05). In conclusion, minocycline produced antidepressant-like actions in the FST and subthreshold dose of minocycline combined with subthreshold dose of desipramine and several glutamate receptor antagonists and produced antidepressant-like actions.
IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(minocycline alone or in combination with glutamate receptor antagonists such as MTEP showed antidepressant-like actions in rat)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



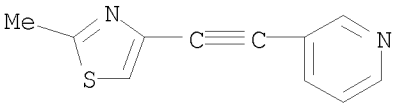
L4 ANSWER 4 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:28700 CAPLUS
DOCUMENT NUMBER: 148:347493
TITLE: Inducible expression and pharmacological characterization of the mouse metabotropic glutamate 5b receptor
AUTHOR(S): Salisbury, Brian G.; Mukhopadhyay, Gitali; Kostich, Mitch; Laz, Thomas M.; Norris, Ellie D.
CORPORATE SOURCE: Neurobiology Research and Discovery Technologies, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
SOURCE: European Journal of Pharmacology (2008), 579(1-3), 34-39
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The metabotropic glutamate receptor subtype 5 (mGlu5) and glutamatergic neurotransmission are associated with the pathophysiol. of disorders such as anxiety, depression, or chronic pain. Human and rat mGlu5 receptors were cloned and characterized previously. The authors now describe the cloning of the mouse mGlu5b receptor gene from adult mouse brain and its expression using an ecdysone-inducible system. This subtype has an extra

96 bp sequence which is inserted to the cytoplasmic tail and is identical to the insert present in human and rat mGlu5b. Mouse mGlu5b receptor expression was induced in HEK-293EcR cells by incubation with ponasterone A, an analog of the insect hormone ecdysone. A fluorometric calcium transient assay system was used to characterize the basic pharmacol. profile of an isolated stable cell line. Quisqualic acid was the most potent receptor agonist (EC50 .apprx. 7 nM) although the cells also responded to L-glutamic acid and the Group I-selective receptor agonist, 3,5-dihydroxyphenylglycine (3,5-DHPG). The calcium transients stimulated by these agonists were potently inhibited by reference allosteric mGlu5 antagonists - 2-methyl-6-(phenylethynyl)pyridine (MPEP), 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (MTEP), and 3-methoxy-5-(pyridine-2-ylethynyl)pyridine (methoxy-PEPy) (IC50 ranges: 0.8-66 nM). The availability of this mouse mGlu5b receptor-expressing cell line will facilitate in vitro characterization of mGlu5 receptor-selective agonists or antagonists prior to in vivo pharmacol. testing.

IT 329205-68-7, 3-[(2-Methyl-1,3-thiazol-4-yl)ethynyl]pyridine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sequence, inducible expression and pharmacol. characterization of mouse metabotropic glutamate 5b receptor)

RN 329205-68-7 CAPLUS

CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1478735 CAPLUS

DOCUMENT NUMBER: 148:105673

TITLE: Recent developments of the PET imaging agents for metabotropic glutamate receptor subtype 5

AUTHOR(S): Yu, Meixiang

CORPORATE SOURCE: PET Center, Banner Alzheimer's Institute, Phoenix, AZ, 85006, USA

SOURCE: Current Topics in Medicinal Chemistry (Sharjah, United Arab Emirates) (2007), 7(18), 1800-1805
CODEN: CTMCCL; ISSN: 1568-0266

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review

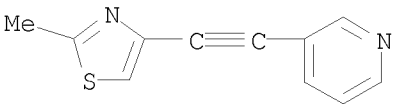
LANGUAGE: English

AB A review. Glutamate is a major excitatory neurotransmitter in central nervous system (CNS) acting through ionotropic and G-protein coupled metabotropic glutamate receptors. Metabotropic glutamate receptor 5 (mGluR5), a subtype in the group I mGluRs, presents in high d. in many brain regions (hippocampus, cortex and olfactory system). Stimulation of mGluR5 leads to the release of calcium from intracellular supplies and protein kinase C activation. Excessive activation of mGluR5 has been associated with psychiatric, neurol. and neurodegenerative diseases, including Parkinson's disease, anxiety, depression, schizophrenia, pain, epilepsy, focal and global ischemia diseases. 2-Methyl-6-(phenylethynyl)pyridine (MPEP) and 2-methyl-4-(pyridin-3-ylethynyl)thiazole (MTEP) are the first generation of non-competitive

mGluR5 antagonists with potent, selective and systemically active properties. They have therapeutic functions in varied diseases. Investigation of mGluR5 physiol. functions under pathol. conditions in patients will be critically important in mGluR5 antagonist's therapy using noninvasive positron emission tomog. (PET) imaging technique. There are eleven mGluR5 imaging PET tracers have been tested in animal studies. This article highlights efforts on the design and development of novel PET tracers for mGluR5 in vivo imaging.

IT 329205-68-7, MTEP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PET imaging agents for metabotropic glutamate receptor subtype 5)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1364083 CAPLUS
DOCUMENT NUMBER: 148:1117
TITLE: Melatonin agonist for treatment of depressive disorders
INVENTOR(S): Wolfgang, Curt D.; Polymeropoulos, Mihael H.
PATENT ASSIGNEE(S): Vanda Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 24pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007137227	A1	20071129	WO 2007-US69373	20070521

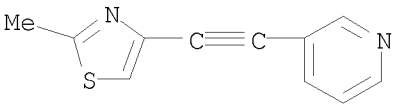
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-747861P P 20060522

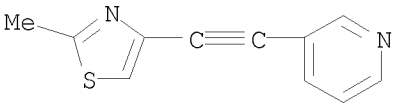
AB A method of treating depression comprising administering a melatonin agonist.

IT 329205-68-7, 3-[(2-Methyl-1,3-thiazol-4-yl)ethynyl]pyridine
329205-68-7D, 3-[(2-Methyl-1,3-thiazol-4-yl)ethynyl]pyridine, metabolites
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(melatonin agonist for treatment of depressive disorders)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

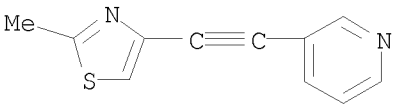


L4 ANSWER 7 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1236736 CAPLUS
DOCUMENT NUMBER: 147:496353
TITLE: Pharmacological modulation of positive AMPA receptor modulator effects on neurotrophin expression
INVENTOR(S): Lauterborn, Julie C.; Gall, Christine M.; Lynch, Gary
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 98pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

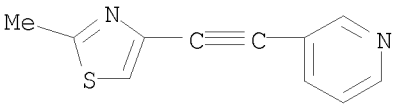
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007124348	A2	20071101	WO 2007-US66947	20070419
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2006-793966P P 20060420
AB Antagonists of group 1 metabotropic glutamate receptors (mGluR) potentiate the effect of pos. AMPA receptor modulators on neurotrophin expression, such as brain-derived neurotrophic factor (BDNF). The findings described herein suggest a combinatorial approach for drug therapies, using both pos. AMPA receptor modulators and mGluR antagonists, to enhance brain neurotrophism.
IT 329205-68-7, MTEP 329205-68-7D, MTEP, analogs

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modulation of pos. AMPA receptor modulator effects on neurotrophin expression)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

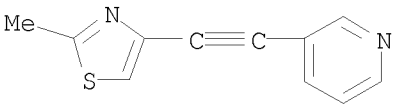


RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



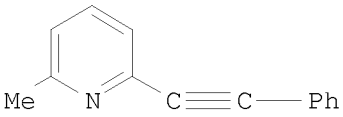
L4 ANSWER 8 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1158232 CAPLUS
DOCUMENT NUMBER: 147:534544
TITLE: Anxiolytic-like action of MTEP expressed in the conflict drinking Vogel test in rats is serotonin dependent
AUTHOR(S): Stachowicz, K.; Golembiowska, K.; Sowa, M.; Nowak, G.; Chojnacka-Wojcik, E.; Pilc, A.
CORPORATE SOURCE: Institute of Pharmacology, Polish Academy of Sciences, Krakow, 31-343, Pol.
SOURCE: Neuropharmacology (2007), 53(6), 741-748
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of the present study was to investigate whether the anxiolytic-like action of a selective and brain penetrable group I metabotropic glutamate (mGlu5) receptor antagonist 3-[(2-methyl-1,3-tiazol-4-yl)ethynyl]-pyridine (MTEP) is dependent upon the serotonergic system. Expts. were performed on male Wistar rats. The Vogel conflict drinking test was used to detect anxiolytic-like activity. MTEP administered i.p. at doses of 1, 3 and 6 mg/kg induced anxiolytic-like effect. The potential anxiolytic effect of MTEP (1 mg/kg) was inhibited by a nonselective 5-HT receptor antagonist metergoline (2 mg/kg i.p.) and 5-HT2A/2C receptor antagonist ritanserin (0.5 mg/kg i.p.), but not by a 5-HT1A receptor antagonist N-{2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl}-N-(2-pyridynyl)cyclohexane-carboxamide (WAY 100635) (0.1 mg/kg i.p). The anxiolytic effect of MTEP (6 mg/kg) was attenuated by ritanserin (1 mg/kg i.p.). Moreover, MTEP-induced a dose-dependent release of serotonin in the frontal cortex. The obtained results suggest that the potential anxiolytic effect of the mGlu5 receptor antagonist MTEP is due to the increased serotonin release with subsequent activation of 5-HT2A/2C receptors, most probably located postsynaptically, but not by the 5-HT1A receptors.
IT 329205-68-7, MTEP

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anxiolytic-like action of MTEP expressed in conflict drinking Vogel test in rats is serotonin dependent)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

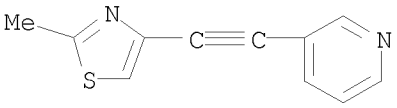
L4 ANSWER 9 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:810134 CAPLUS
DOCUMENT NUMBER: 147:291358
TITLE: Rational design of 7-arylquinolines as non-competitive metabotropic glutamate receptor subtype 5 antagonists
AUTHOR(S): Milbank, Jared B. J.; Knauer, Christopher S.; Augelli-Szafran, Corinne E.; Sakkab-Tan, Annette T.; Lin, Kristin K.; Yamagata, Koji; Hoffman, Jennifer K.; Zhuang, Nian; Thomas, John; Galatsis, Paul; Wendt, John A.; Mickelson, John W.; Schwarz, Roy D.; Kinsora, Jack J.; Lotarski, Susan M.; Stakich, Korana; Gillespie, Kristen K.; Lam, Wing W.; Mutlib, Abdul E.
CORPORATE SOURCE: Michigan Laboratories, Pfizer Global Research and Development, Ann Arbor, MI, 48105, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2007), 17(16), 4415-4418
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 147:291358
GI



I

AB Rational replacement of the alkyne linker of mGluR5 antagonist MPEP (I) gave 7-arylquinolines. SAR optimization gave an orally active compound with high affinity for the MPEP binding site.
IT 329205-68-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(arylquinolines as non-competitive metabotropic glutamate receptor subtype 5 antagonists)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:730875 CAPLUS
DOCUMENT NUMBER: 147:143429
TITLE: Preparation of phenoxypiperidines and analogs thereof useful as histamine H3 antagonists
INVENTOR(S): Mutahi, Mwangi W.; Aslanian, Robert G.; Berlin, Michael Y.; Boyce, Christopher W.; De Lera Ruiz, Manuel; McCormick, Kevin D.; Solomon, Daniel M.; Vaccaro, Henry A.; Zheng, Junying; Purakkattle, Biju J.; Yu, Younong; Zhou, Wei; Zhu, Xiaohong
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 127pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007075629	A2	20070705	WO 2006-US48349	20061219
WO 2007075629	A3	20071018		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
US 20070167435	A1	20070719	US 2006-641175	20061219
PRIORITY APPLN. INFO.:			US 2005-752636P P	20051221
OTHER SOURCE(S):	MARPAT 147:143429			

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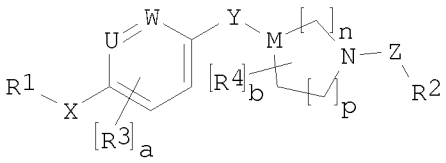

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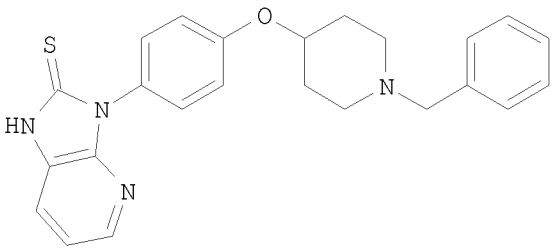


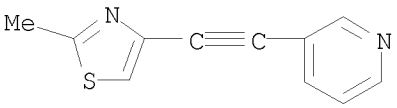
II

AB The title compds. I [a = 0-4; b = 0-3; M = CH or N; U and W are each CH, or one of U and W is CH and the other is N; X = bond, alkylene, C(O), etc. Y = O, (CH2)2, C(O), C(:NOR7) or SO0-2; Z = a bond, (un)substituted alkylene or alkylene interrupted by a heteroatom or heterocyclic group; R1 = (un)substituted alkyl, cycloalkyl, aryl, arylalkyl, heteroaryl, heterocycloalkyl, or benzimidazolyl or a derivative thereof; R2 = (un)substituted alkyl, alkenyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl or heterocycloalkyl; R3 = H, alkyl, halo, OH, alkoxy, etc.; R4 = H, halo, alkyl, haloalkyl, OH, alkoxy, CF3 and CN; R7 = H, alkyl, haloalkyl, etc.; n = 1-2; p = 0-2; and their pharmaceutically acceptable salts], useful for treating an allergy-induced airway response, congestion, diabetes, obesity, an obesity-related disorder, metabolic syndrome and a cognition deficit disorder, were prepared E.g., a multi-step synthesis of II, starting from 4-fluoronitrobenzene and N-(tert-butoxycarbonyl)-4-piperidinol, was given. Compds. I have a Ki within the range of about 0.6 to about 600 nM at the recombinant human H3 receptor and from about 18 nM to about 400 nM at the guinea pig brain receptor. Pharmaceutical composition comprising compound I alone or in combination with other agents are disclosed.

IT 329205-68-7, 3-[(2-Methyl-1,3-thiazol-4-yl)ethynyl]pyridine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(addnl. therapeutic agent; preparation of phenoxypiperidines and analogs useful as histamine H3 antagonists for treating various disorders)

RN 329205-68-7 CAPLUS

CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



L4 ANSWER 11 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:649624 CAPLUS
DOCUMENT NUMBER: 147:257686
TITLE: Synthesis and Simple 18F-Labeling of

	3-Fluoro-5-(2-(2-(fluoromethyl)thiazol-4-yl)ethynyl)benzonitrile as a High Affinity Radioligand for Imaging Monkey Brain Metabotropic Glutamate Subtype-5 Receptors with Positron Emission Tomography
AUTHOR(S):	Simeon, Fabrice G.; Brown, Amira K.; Zoghbi, Sami S.; Patterson, Velvet M.; Innis, Robert B.; Pike, Victor W.
CORPORATE SOURCE:	Molecular Imaging Branch, National Institute of Mental Health, Bethesda, MD, 20892-1003, USA
SOURCE:	Journal of Medicinal Chemistry (2007), 50(14), 3256-3266 CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 147:257686

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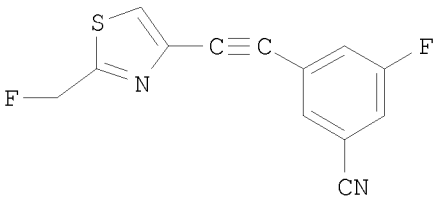


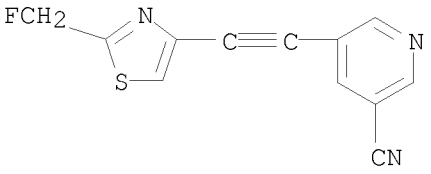
I

AB 2-Fluoromethyl analogs of (3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine) were synthesized as potential ligands for metabotropic glutamate subtype-5 receptors (mGluR5s). One of these, namely, 3-fluoro-5-(2-(2-(fluoromethyl)thiazol-4-yl)ethynyl)benzonitrile (I), was found to have exceptionally high affinity (IC50 = 36 pM) and potency in a phosphoinositol hydrolysis assay (IC50 = 0.714 pM) for mGluR5. Compound I was labeled with fluorine-18 (t1/2 = 109.7 min) in high radiochem. yield (87%) by treatment of its synthesized bromomethyl analog with [18F]fluoride ion and its radioligand behavior was assessed with positron emission tomog. (PET). Following i.v. injection of [18F]I into rhesus monkey, radioactivity was avidly taken up into brain with high uptake in mGluR5 receptor-rich regions such as striata. [18F]I was stable in monkey plasma and human whole blood in vitro and in monkey and human brain homogenates. In monkey in vivo, a single polar radiometabolite of [18F]I appeared rapidly in plasma. [18F]I merits further evaluation as a PET radioligand for mGluR5 in human subjects.

IT 945933-45-9P
RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and 18F-labeling of 3-fluoro-5-(2-(2-(fluoromethyl)thiazol-4-yl)ethynyl)benzonitrile as a high affinity radioligand for imaging monkey brain metabotropic glutamate subtype-5 receptors with positron emission tomog.)

RN 945933-45-9 CAPLUS

CN 3-Pyridinecarbonitrile, 5-[2-[2-(fluoromethyl)-4-thiazolyl]ethynyl]- (CA INDEX NAME)



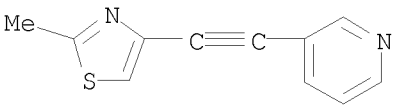
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:544367 CAPLUS
DOCUMENT NUMBER: 147:158237
TITLE: Neuroprotective effects of MTEP, a selective mGluR5 antagonist and neuropeptide Y on the kainate-induced toxicity in primary neuronal cultures
AUTHOR(S): Domin, Helena; Kajta, Malgorzata; Smialowska, Maria
CORPORATE SOURCE: Department of Neurobiology, Institute of Pharmacology, Polish Academy of Sciences, Krakow, PL 31-343, Pol.
SOURCE: Pharmacological Reports (2006), 58(6), 846-858
CODEN: PRHEDU; ISSN: 1734-1140
PUBLISHER: Polish Academy of Sciences, Institute of Pharmacology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The majority of studies on neuroprotection tested potentially protective compds. given before, simultaneously or shortly after damage. Such procedures are greatly different from the situation faced in clin. practice. In the present study, we tried to find out whether two compds., a selective mGluR5 antagonist 3-[(2-methyl-1,3-thiazol-4-yl) ethynyl]-pyridine (MTEP) and neuropeptide Y (NPY) elicit neuroprotective action against excitotoxic damage in the mouse neocortical and hippocampal neuronal cultures after delayed treatment. In order to evoke toxic effects, primary cultures were exposed to 150 μM kainic acid (KA) for 24 h (hippocampus) or for 48 h (neocortex). MTEP (1, 10 and 100 μM), or NPY (0.5 μM and 1 μM) were applied 30 min before, or 30 min, 1 h, 3 h or 6 h after KA. Kainate neurotoxicity was measured by lactate dehydrogenase (LDH) efflux from the damaged cells into the culture media. The results of our studies showed that MTEP or NPY treatment attenuated the kainate-induced LDH release in mouse neocortical and hippocampal cultures. The effect was observed when the compds. were added not only before, but also 30 min to 6 h after KA. Moreover, both MTEP and NPY displayed antiapoptotic activity as they prevented the KA-induced increase in the expression of caspase-3 activity in the cultures under study. Summing up, our data showed that MTEP and NPY were neuroprotective in wide time schedule. The effectiveness of late treatment with these compds. opens a new perspective for their potential therapeutic use.

IT 329205-68-7, 3-[(2-Methyl-1, 3-thiazol-4-yl) ethynyl]-pyridine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3-[(2-methyl-1, 3-thiazol-4-yl) ethynyl]-pyridine attenuated kainic acid-induced lactate dehydrogenase release and prevented caspase-3 activity in mouse neocortical and hippocampal primary neuronal culture)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

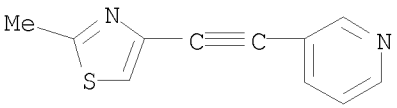


REFERENCE COUNT: 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:506160 CAPLUS
DOCUMENT NUMBER: 147:87290
TITLE: Antagonism of metabotropic glutamate receptor type 5 attenuates L-DOPA-induced dyskinesia and its molecular and neurochemical correlates in a rat model of Parkinson's disease
AUTHOR(S): Mela, Flora; Marti, Matteo; Dekundy, Andrzej; Danysz, Wojciech; Morari, Michele; Cenci, M. Angela
CORPORATE SOURCE: Basal Ganglia Pathophysiology Unit, Department of Experimental Medical Science, Lund University, Lund, Swed.
SOURCE: Journal of Neurochemistry (2007), 101(2), 483-497
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Metabotropic glutamate receptor type 5 (mGluR5) modulates dopamine and glutamate neurotransmission at central synapses. In this study, we addressed the role of mGluR5 in L-DOPA-induced dyskinesia, a movement disorder that is due to abnormal activation of both dopamine and glutamate receptors in the basal ganglia. A selective and potent mGluR5 antagonist, 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl] pyridine, was tested for its ability to modulate mol., behavioral and neurochem. correlates of dyskinesia in 6-hydroxydopamine-lesioned rats treated with L-DOPA. The compound significantly attenuated the induction of abnormal involuntary movements (AIMs) by chronic L-DOPA treatment at doses that did not interfere with the rat physiol. motor activities. These effects were paralleled by an attenuation of mol. changes that are strongly associated with the dyskinesiogenic action of L-DOPA (i.e. up-regulation of prodynorphin mRNA in striatal neurons). Using in vivo microdialysis, we found a temporal correlation between the expression of L-DOPA-induced AIMs and an increased GABA outflow within the substantia nigra pars reticulata. When co-administered with L-DOPA, 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl] pyridine greatly attenuated both the increase in nigral GABA levels and the expression of AIMs. These data demonstrate that mGluR5 antagonism produces strong anti-dyskinetic effects in an animal model of Parkinson's disease through central inhibition of the mol. and neurochem. underpinnings of L-DOPA-induced dyskinesia.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antagonism of mGluR5 attenuates DOPA-induced dyskinesia)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:486155 CAPLUS
DOCUMENT NUMBER: 146:482054
TITLE: Thiazolyl derivatives as mGluR5 antagonists and their preparation and methods for their use
INVENTOR(S): Cosford, Nicholas D.; Seiders, Thomas J.; Payne, Joseph; Roppe, Jeffrey R.; Huang, Dehua; Smith, Nicholas D.; Poon, Steve F.; King, Chris; Eastman, Brian W.; Wang, Bowei; Arruda, Jeannie M.; Vernier, Jean-Michel; Zhao, Xiumin
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2007050050	A2	20070503	WO 2005-US35921		20051006
WO 2007050050	A3	20080207			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA					
CA 2583572	A1	20060407	CA 2005-2583572		20051006
AU 2005336513	A1	20070517	AU 2005-336513		20051006
EP 1893608	A2	20080305	EP 2005-858618		20051006
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR					
JP 2008516004	T	20080515	JP 2007-543041		20051006
IN 2007CN01215	A	20070831	IN 2007-CN1215		20070323
PRIORITY APPLN. INFO.:			US 2004-616805P	P	20041007
			WO 2005-US35921	W	20051006

OTHER SOURCE(S): MARPAT 146:482054
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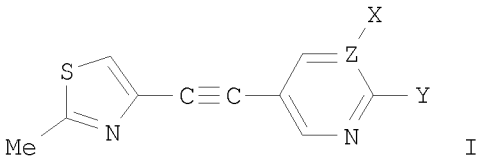

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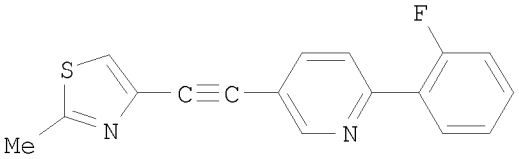

II

AB The identification of a unique series of compds. of formula I, which possesses special advantages in terms of drug-like properties due to their possessing advantageous properties in terms of potency and/or pharmacokinetic and/or selectivity and/or in vivo receptor occupancy properties. Compds. of formula I wherein Z is C or N; when Z is N, X is absent; X is H; and Y is (un)substituted (hetero)aryl, amino, alkoxy, alkylthio, etc.; or Y is H; and X is (un)substituted (hetero)aryl, halo, cycloalkyl, alkenyl, amino, etc.; and their radioisotopes and pharmaceutically acceptable salts thereof are claimed. Specifically, the selection of a 1,3-thiazol-2-yl ring member linked by an ethynylene to the 3 position of a pyridyl ring or the 5 position of a pyrimidinyl ring, wherein the ring is substituted with selected substituents, results in a compound having superior drug-like properties. The invention includes pharmaceutically acceptable salt forms of these heterocyclic compds., in particular chloride salts and trifluoroacetate salts. Example compound II was prepared by cross-coupling of 2-chloro-5-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine with 2-fluorophenylboronic acid. All the invention compds. were evaluated for their mGluR5 antagonistic activity. From the assay, it was determined that compound II exhibited a Ki value of 2.0 nM.

IT 524924-78-5P 878018-89-4P 935684-55-2P
935684-56-3P 935684-57-4P 935684-58-5P
935684-59-6P 935684-60-9P 935684-61-0P
935684-62-1P 935684-64-3P 935684-66-5P
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935684-90-5P 935684-92-7P 935684-93-8P
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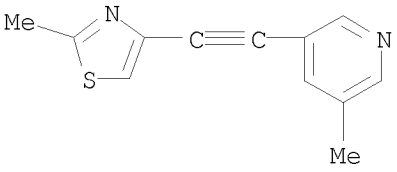
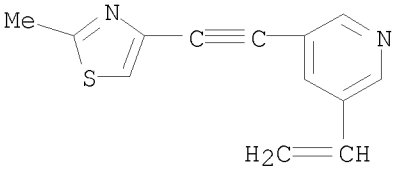
935685-95-3P 935685-96-4P 935685-97-5P
935685-98-6P 935686-20-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of (thiazolylethynyl)pyridines and -pyrimidines as mGluR5 antagonists)

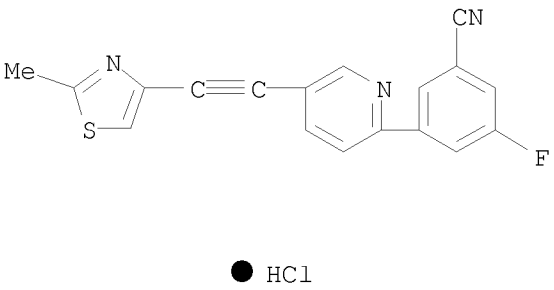
RN 524924-78-5 CAPLUS
CN Pyridine, 3-methyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



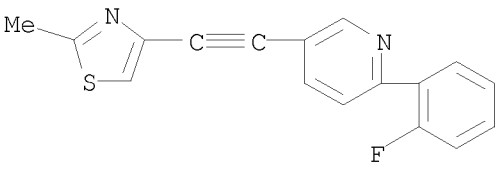
RN 878018-89-4 CAPLUS
CN Pyridine, 3-ethenyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 935684-55-2 CAPLUS
CN Benzonitrile, 3-fluoro-5-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, hydrochloride (1:1) (CA INDEX NAME)

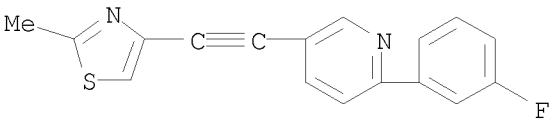


RN 935684-56-3 CAPLUS
CN Pyridine, 2-(2-fluorophenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:1) (CA INDEX NAME)



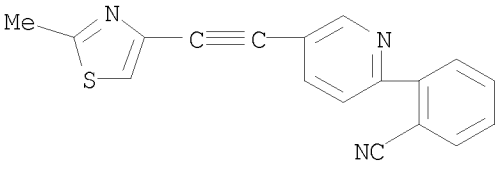
● HCl

RN 935684-57-4 CAPLUS
CN Pyridine, 2-(3-fluorophenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:1) (CA INDEX NAME)



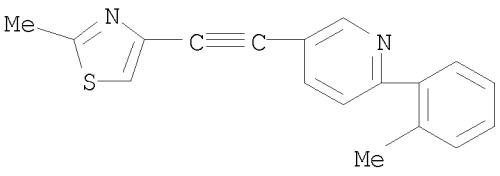
● HCl

RN 935684-58-5 CAPLUS
CN Benzonitrile, 2-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, hydrochloride (1:1) (CA INDEX NAME)



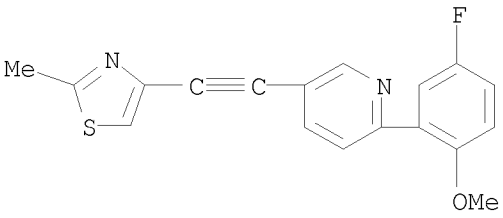
● HCl

RN 935684-59-6 CAPLUS
CN Pyridine, 2-(2-methylphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:1) (CA INDEX NAME)



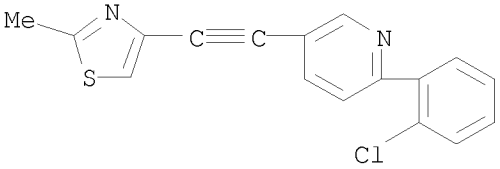
● HCl

RN 935684-60-9 CAPLUS
CN Pyridine, 2-(5-fluoro-2-methoxyphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:1) (CA INDEX NAME)



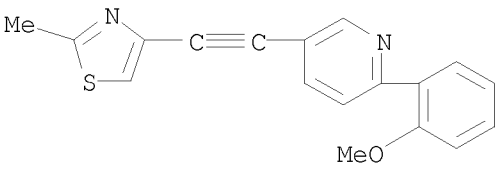
● HCl

RN 935684-61-0 CAPLUS
CN Pyridine, 2-(2-chlorophenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 935684-62-1 CAPLUS
CN Pyridine, 2-(2-methoxyphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:1) (CA INDEX NAME)

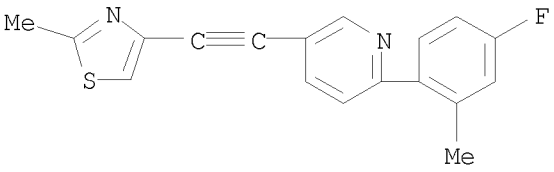


● HCl

RN 935684-64-3 CAPLUS
CN Pyridine, 2-(4-fluoro-2-methylphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

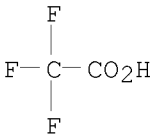
CM 1

CRN 935684-63-2
CMF C18 H13 F N2 S



CM 2

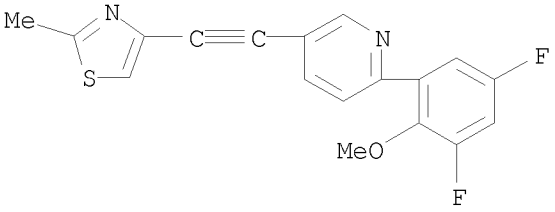
CRN 76-05-1
CMF C2 H F3 O2



RN 935684-66-5 CAPLUS
CN Pyridine, 2-(3,5-difluoro-2-methoxyphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

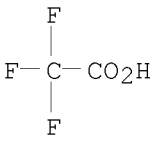
CM 1

CRN 935684-65-4
CMF C18 H12 F2 N2 O S



CM 2

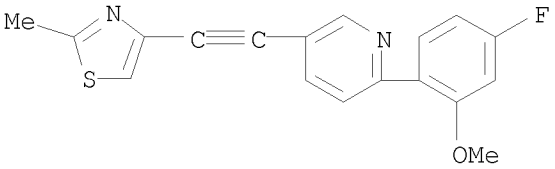
CRN 76-05-1
CMF C2 H F3 O2



RN 935684-68-7 CAPLUS
CN Pyridine, 2-(4-fluoro-2-methoxyphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

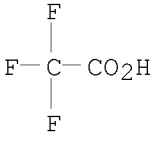
CM 1

CRN 935684-67-6
CMF C18 H13 F N2 O S



CM 2

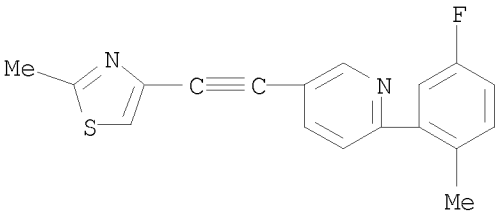
CRN 76-05-1
CMF C2 H F3 O2



RN 935684-70-1 CAPLUS
CN Pyridine, 2-(5-fluoro-2-methylphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

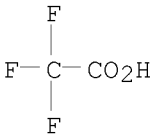
CM 1

CRN 935684-69-8
CMF C18 H13 F N2 S

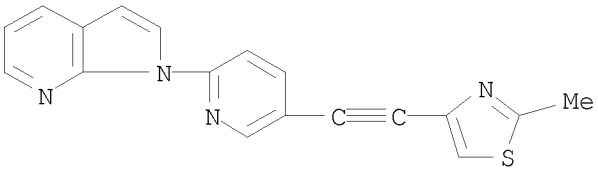


CM 2

CRN 76-05-1
CMF C2 H F3 O2

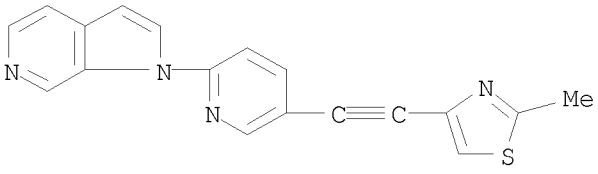


RN 935684-75-6 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 1-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, hydrochloride (1:1) (CA INDEX NAME)



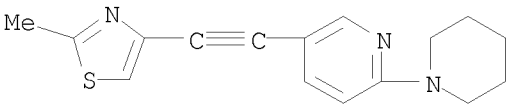
● HCl

RN 935684-76-7 CAPLUS
CN 1H-Pyrrolo[2,3-c]pyridine, 1-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, hydrochloride (1:1) (CA INDEX NAME)



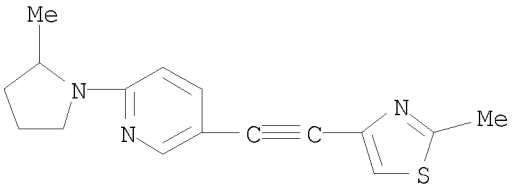
● HCl

RN 935684-77-8 CAPLUS
CN Pyridine, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-(1-piperidinyl)-, hydrochloride (1:1) (CA INDEX NAME)



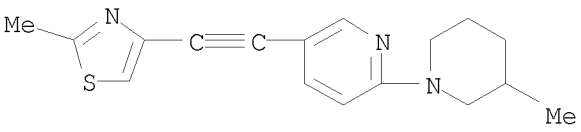
● HCl

RN 935684-78-9 CAPLUS
CN Pyridine, 2-(2-methyl-1-pyrrolidinyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:1) (CA INDEX NAME)



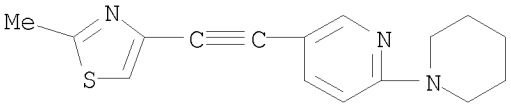
● HCl

RN 935684-82-5 CAPLUS
CN Pyridine, 2-(3-methyl-1-piperidinyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

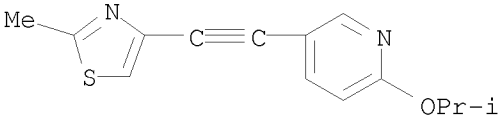


RN 935684-83-6 CAPLUS
CN Pyridine, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-(1-piperidinyl)- (CA

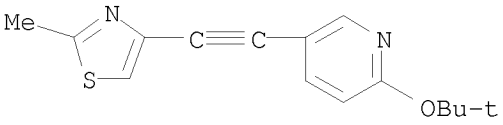
INDEX NAME)



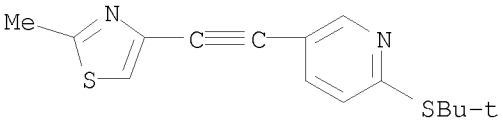
RN 935684-85-8 CAPLUS
CN Pyridine, 2-(1-methylethoxy)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



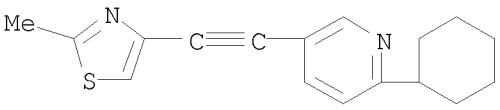
RN 935684-86-9 CAPLUS
CN Pyridine, 2-(1,1-dimethylethoxy)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 935684-87-0 CAPLUS
CN Pyridine, 2-[(1,1-dimethylethyl)thio]-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

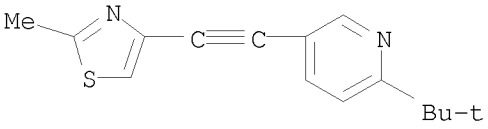


RN 935684-89-2 CAPLUS
CN Pyridine, 2-cyclohexyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:1) (CA INDEX NAME)

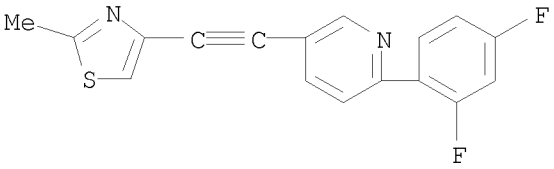


● HCl

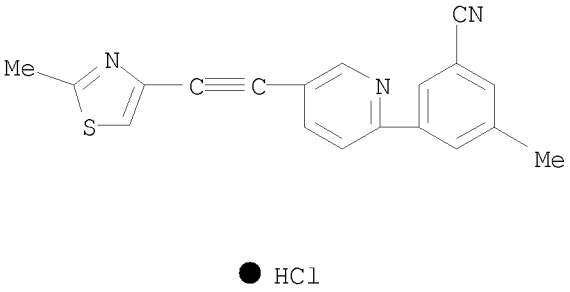
RN 935684-90-5 CAPLUS
CN Pyridine, 2-(1,1-dimethylethyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



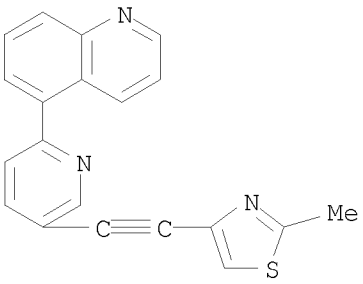
RN 935684-92-7 CAPLUS
CN Pyridine, 2-(2,4-difluorophenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



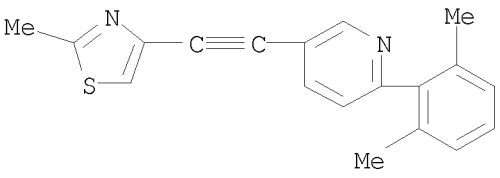
RN 935684-93-8 CAPLUS
CN Benzonitrile, 3-methyl-5-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, hydrochloride (1:1) (CA INDEX NAME)



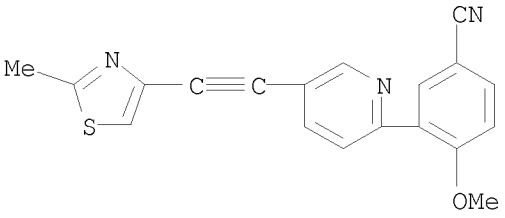
RN 935684-94-9 CAPLUS
CN Quinoline, 5-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]- (CA INDEX NAME)



RN 935684-95-0 CAPLUS
CN Pyridine, 2-(2,6-dimethylphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

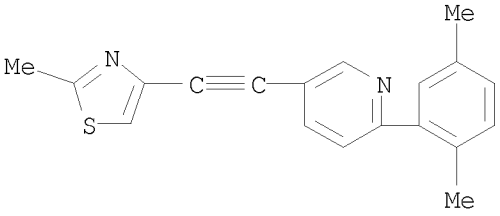


RN 935684-96-1 CAPLUS
CN Benzonitrile, 4-methoxy-3-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, hydrochloride (1:1) (CA INDEX NAME)

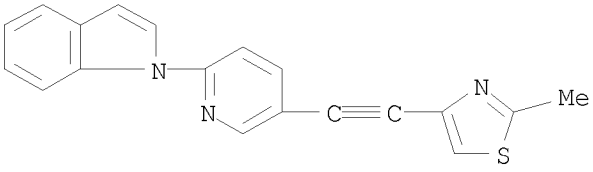


● HCl

RN 935684-97-2 CAPLUS
CN Pyridine, 2-(2,5-dimethylphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 935684-98-3 CAPLUS
CN 1H-Indole, 1-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, hydrochloride (1:1) (CA INDEX NAME)

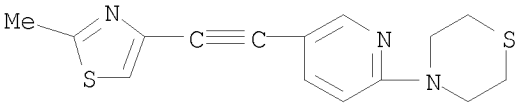


● HCl

RN 935685-00-0 CAPLUS
CN Thiomorpholine, 4-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

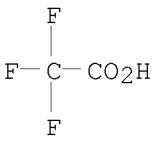
CM 1

CRN 935684-99-4
CMF C15 H15 N3 S2

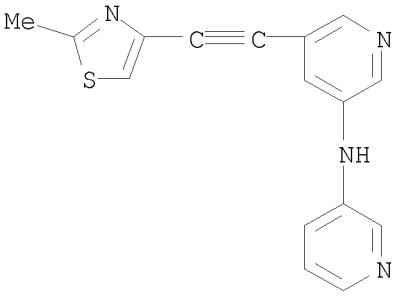


CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 935685-01-1 CAPLUS
CN 3-Pyridinamine, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-N-3-pyridinyl-, hydrochloride (1:1) (CA INDEX NAME)

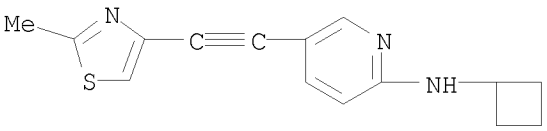


● HCl

RN 935685-03-3 CAPLUS
CN 2-Pyridinamine, N-cyclobutyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

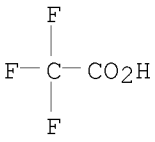
CM 1

CRN 935685-02-2
CMF C15 H15 N3 S

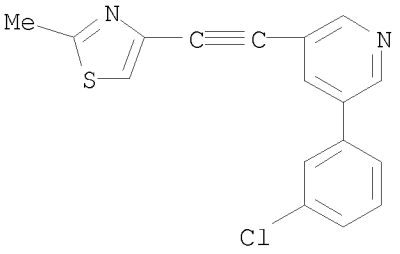


CM 2

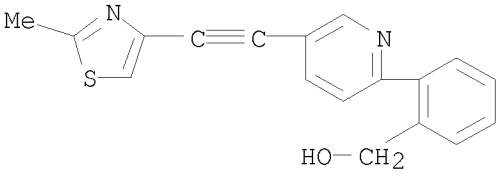
CRN 76-05-1
CMF C2 H F3 O2



RN 935685-04-4 CAPLUS
CN Pyridine, 3-(3-chlorophenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

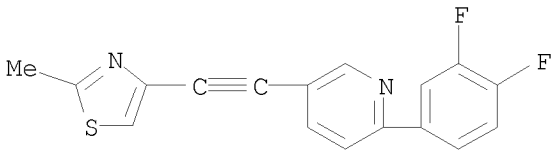


RN 935685-05-5 CAPLUS
CN Benzenemethanol, 2-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, hydrochloride (1:1) (CA INDEX NAME)

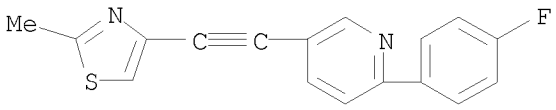


● HCl

RN 935685-06-6 CAPLUS
CN Pyridine, 2-(3,4-difluorophenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

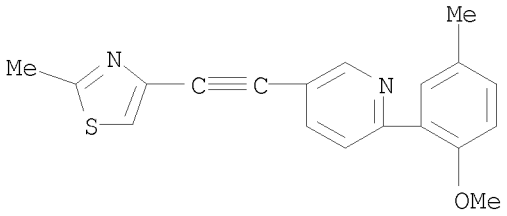


RN 935685-07-7 CAPLUS
CN Pyridine, 2-(4-fluorophenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:2) (CA INDEX NAME)

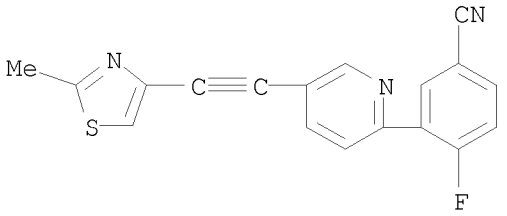


●2 HCl

RN 935685-08-8 CAPLUS
CN Pyridine, 2-(2-methoxy-5-methylphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

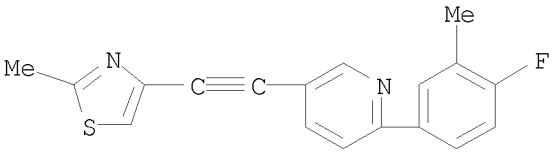


RN 935685-09-9 CAPLUS
CN Benzonitrile, 4-fluoro-3-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, hydrochloride (1:1) (CA INDEX NAME)

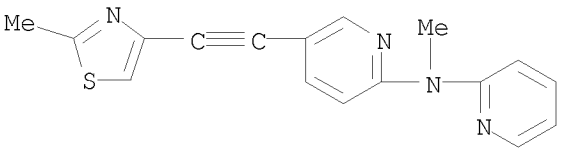


● HCl

RN 935685-10-2 CAPLUS
CN Pyridine, 2-(4-fluoro-3-methylphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

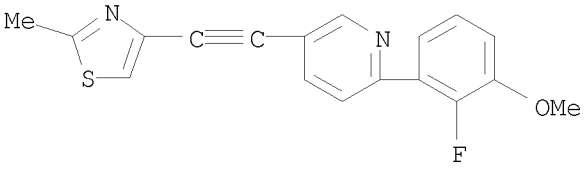


RN 935685-11-3 CAPLUS
CN 2-Pyridinamine, N-methyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]-N-2-pyridinyl-, hydrochloride (1:1) (CA INDEX NAME)

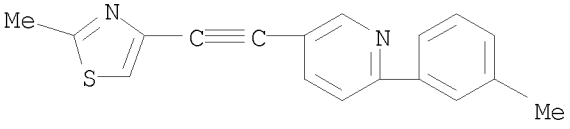


● HCl

RN 935685-12-4 CAPLUS
CN Pyridine, 2-(2-fluoro-3-methoxyphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



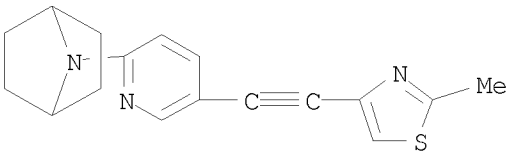
RN 935685-13-5 CAPLUS
CN Pyridine, 2-(3-methylphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 935685-15-7 CAPLUS
CN 7-Azabicyclo[2.2.1]heptane, 7-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

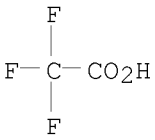
CM 1

CRN 935685-14-6
CMF C17 H17 N3 S

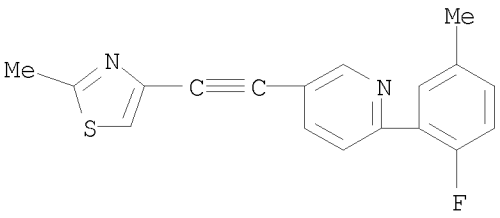


CM 2

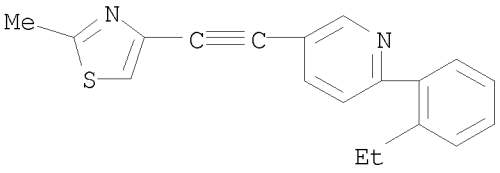
CRN 76-05-1
CMF C2 H F3 O2



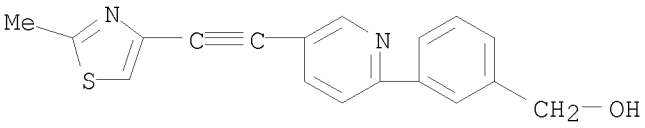
RN 935685-16-8 CAPLUS
CN Pyridine, 2-(2-fluoro-5-methylphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



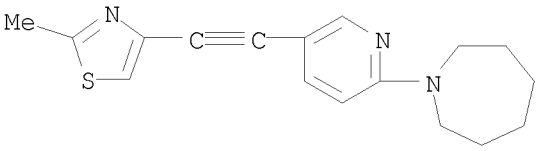
RN 935685-17-9 CAPLUS
CN Pyridine, 2-(2-ethylphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 935685-18-0 CAPLUS
CN Benzenemethanol, 3-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]- (CA INDEX NAME)



RN 935685-19-1 CAPLUS
CN 1H-Azepine, hexahydro-1-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, hydrochloride (1:1) (CA INDEX NAME)

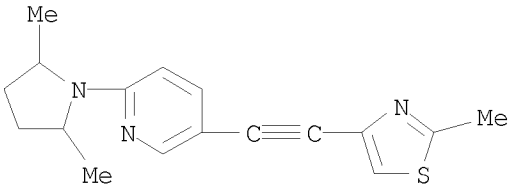


● HCl

RN 935685-21-5 CAPLUS
CN Pyridine, 2-(2,5-dimethyl-1-pyrrolidinyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

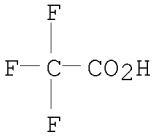
CM 1

CRN 935685-20-4
CMF C17 H19 N3 S



CM 2

CRN 76-05-1
CMF C2 H F3 O2

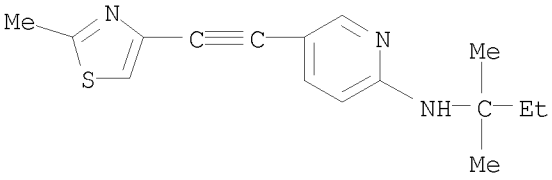


RN 935685-23-7 CAPLUS
CN 2-Pyridinamine, N-(1,1-dimethylpropyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-

, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

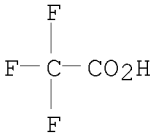
CM 1

CRN 935685-22-6
CMF C16 H19 N3 S



CM 2

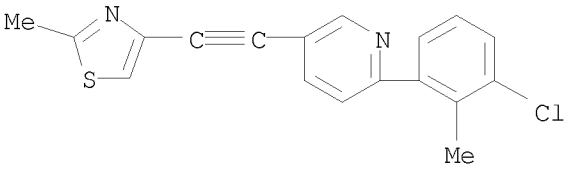
CRN 76-05-1
CMF C2 H F3 O2



RN 935685-25-9 CAPLUS
CN Pyridine, 2-(3-chloro-2-methylphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-
, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

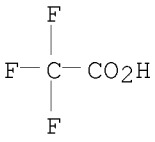
CM 1

CRN 935685-24-8
CMF C18 H13 Cl N2 S



CM 2

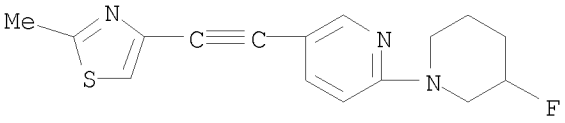
CRN 76-05-1
CMF C2 H F3 O2



RN 935685-27-1 CAPLUS
CN Pyridine, 2-(3-fluoro-1-piperidinyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

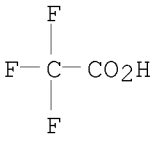
CM 1

CRN 935685-26-0
CMF C16 H16 F N3 S



CM 2

CRN 76-05-1
CMF C2 H F3 O2

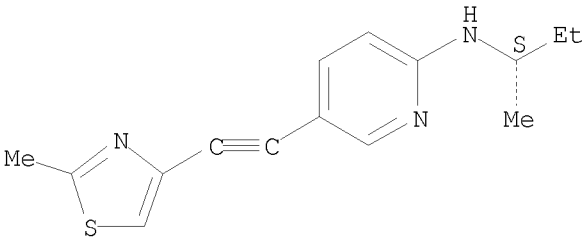


RN 935685-29-3 CAPLUS
CN 2-Pyridinamine, N-[(1S)-1-methylpropyl]-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

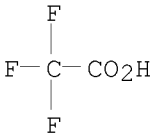
CRN 935685-28-2
CMF C15 H17 N3 S

Absolute stereochemistry.

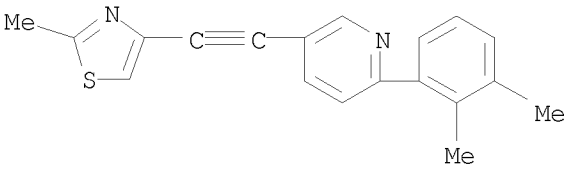


CM 2

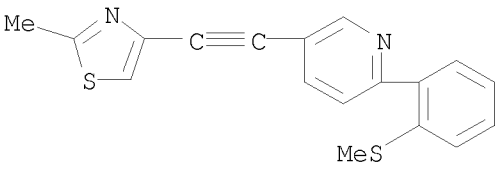
CRN 76-05-1
CMF C2 H F3 O2



RN 935685-30-6 CAPLUS
CN Pyridine, 2-(2,3-dimethylphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

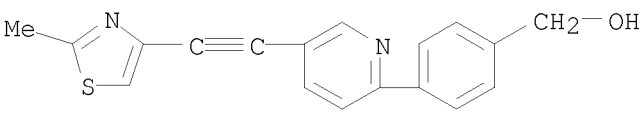


RN 935685-31-7 CAPLUS
CN Pyridine, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-[2-(methylthio)phenyl]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 935685-32-8 CAPLUS
CN Benzenemethanol, 4-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, hydrochloride (1:2) (CA INDEX NAME)



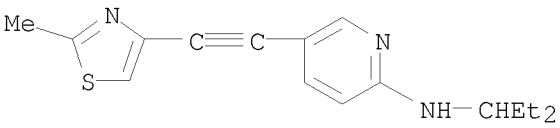
● 2 HCl

RN 935685-34-0 CAPLUS

CN 2-Pyridinamine, N-(1-ethylpropyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

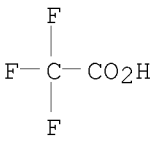
CM 1

CRN 935685-33-9
CMF C16 H19 N3 S

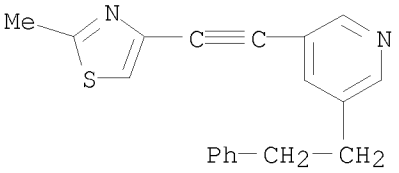


CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 935685-35-1 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]-5-(2-phenylethyl)- (CA INDEX NAME)

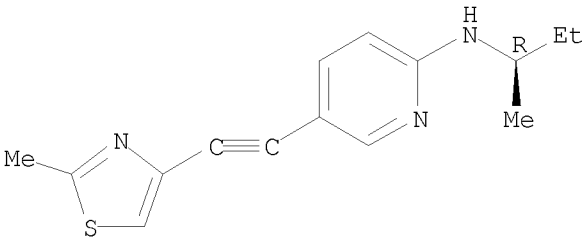


RN 935685-37-3 CAPLUS
CN 2-Pyridinamine, N-[(1R)-1-methylpropyl]-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

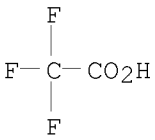
CRN 935685-36-2
CMF C15 H17 N3 S

Absolute stereochemistry.

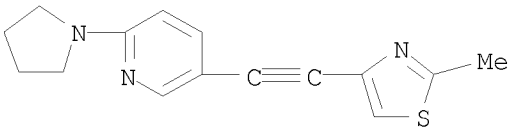


CM 2

CRN 76-05-1
CMF C2 H F3 O2

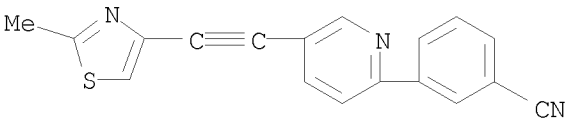


RN 935685-38-4 CAPLUS
CN Pyridine, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-(1-pyrrolidinyl)-, hydrochloride (1:1) (CA INDEX NAME)



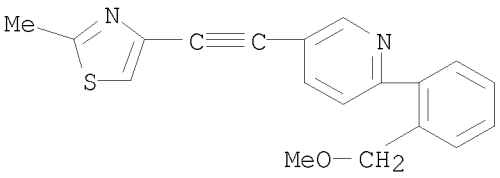
● HCl

RN 935685-39-5 CAPLUS
CN Benzonitrile, 3-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 935685-40-8 CAPLUS
CN Pyridine, 2-[2-(methoxymethyl)phenyl]-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:1) (CA INDEX NAME)

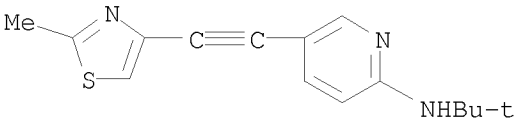


● HCl

RN 935685-42-0 CAPLUS
CN 2-Pyridinamine, N-(1,1-dimethylethyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

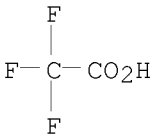
CM 1

CRN 935685-41-9
CMF C15 H17 N3 S

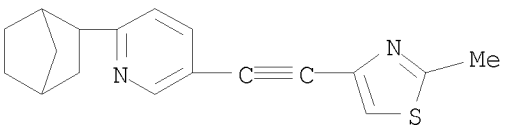


CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 935685-43-1 CAPLUS
CN Pyridine, 2-bicyclo[2.2.1]hept-2-yl-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:1) (CA INDEX NAME)

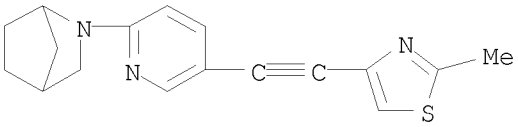


● HCl

RN 935685-45-3 CAPLUS
CN 2-Azabicyclo[2.2.1]heptane, 2-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

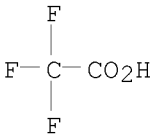
CM 1

CRN 935685-44-2
CMF C17 H17 N3 S

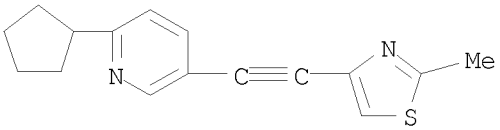


CM 2

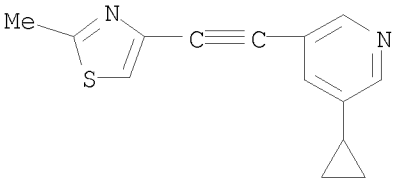
CRN 76-05-1
CMF C2 H F3 O2



RN 935685-46-4 CAPLUS
CN Pyridine, 2-cyclopentyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

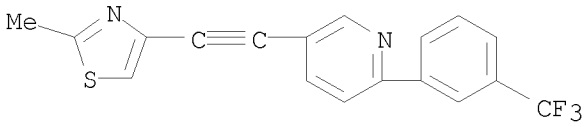


RN 935685-47-5 CAPLUS
CN Pyridine, 3-cyclopropyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:2) (CA INDEX NAME)

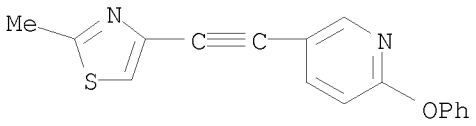


●2 HCl

RN 935685-48-6 CAPLUS
CN Pyridine, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

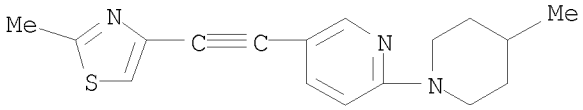


RN 935685-49-7 CAPLUS
CN Pyridine, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-phenoxy-, hydrochloride (1:1) (CA INDEX NAME)

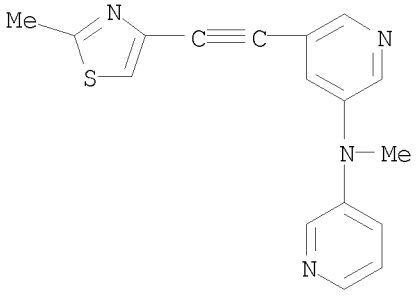


● HCl

RN 935685-50-0 CAPLUS
CN Pyridine, 2-(4-methyl-1-piperidinyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

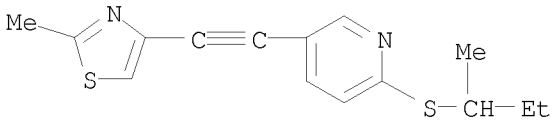


RN 935685-51-1 CAPLUS
CN 3-Pyridinamine, N-methyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]-N-3-pyridinyl-, hydrochloride (1:1) (CA INDEX NAME)



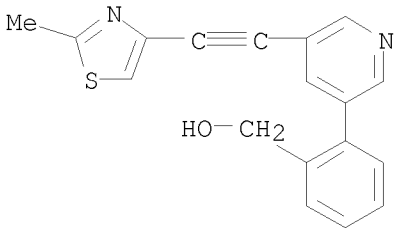
● HCl

RN 935685-52-2 CAPLUS
CN Pyridine, 2-[(1-methylpropyl)thio]-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, conjugate acid (1:1) (CA INDEX NAME)



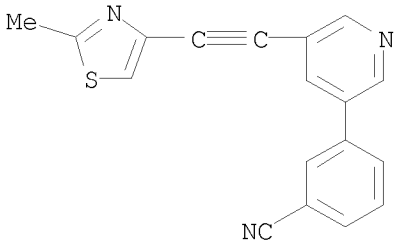
● H^+

RN 935685-53-3 CAPLUS
CN Benzenemethanol, 2-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-3-pyridinyl]-, hydrochloride (1:1) (CA INDEX NAME)

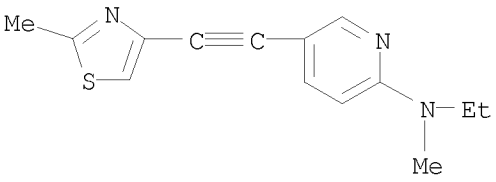


● HCl

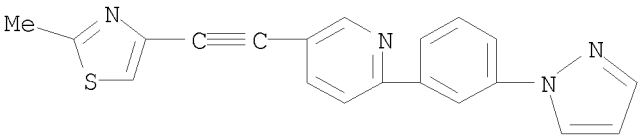
RN 935685-54-4 CAPLUS
CN Benzonitrile, 3-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-3-pyridinyl]- (CA INDEX NAME)



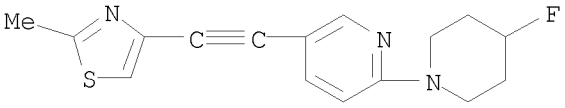
RN 935685-55-5 CAPLUS
CN 2-Pyridinamine, N-ethyl-N-methyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



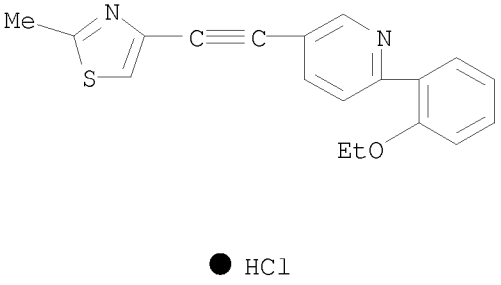
RN 935685-56-6 CAPLUS
CN Pyridine, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-[3-(1H-pyrazol-1-yl)phenyl]- (CA INDEX NAME)



RN 935685-57-7 CAPLUS
CN Pyridine, 2-(4-fluoro-1-piperidinyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

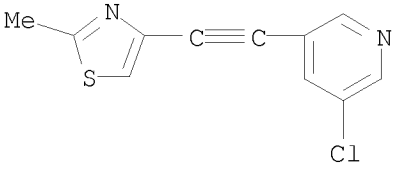


RN 935685-58-8 CAPLUS
CN Pyridine, 2-(2-ethoxyphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:1) (CA INDEX NAME)

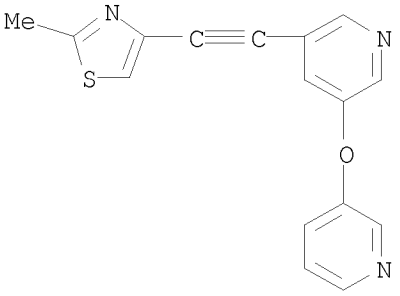


● HCl

RN 935685-59-9 CAPLUS
CN Pyridine, 3-chloro-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

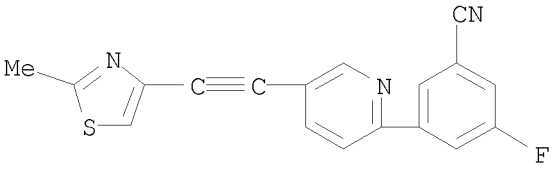


RN 935685-60-2 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]-5-(3-pyridinyloxy)-, hydrochloride (1:1) (CA INDEX NAME)

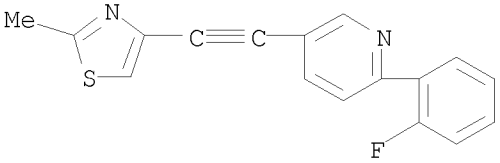


● HCl

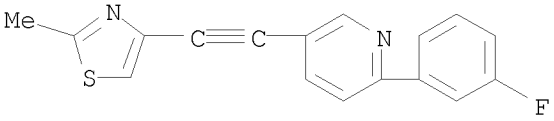
RN 935685-90-8 CAPLUS
CN Benzonitrile, 3-fluoro-5-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]- (CA INDEX NAME)



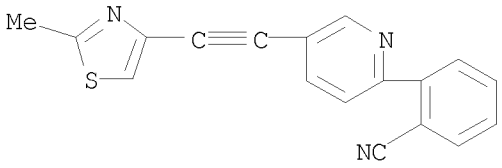
RN 935685-91-9 CAPLUS
CN Pyridine, 2-(2-fluorophenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



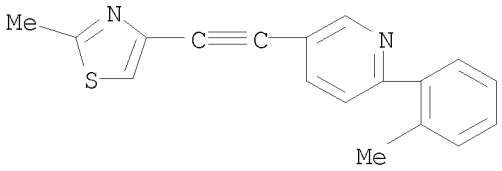
RN 935685-92-0 CAPLUS
CN Pyridine, 2-(3-fluorophenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



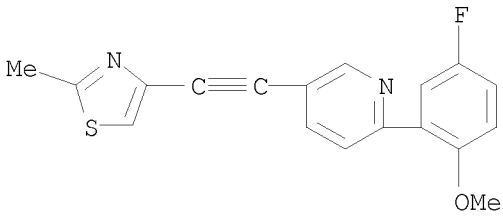
RN 935685-93-1 CAPLUS
CN Benzonitrile, 2-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]- (CA INDEX NAME)



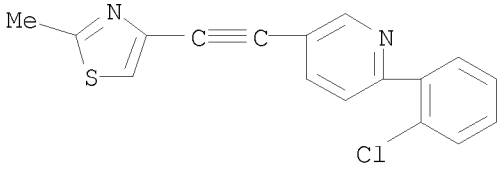
RN 935685-94-2 CAPLUS
CN Pyridine, 2-(2-methylphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



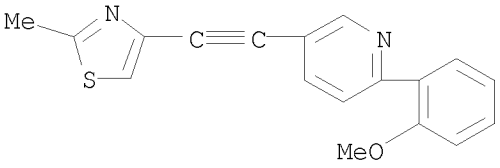
RN 935685-95-3 CAPLUS
CN Pyridine, 2-(5-fluoro-2-methoxyphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



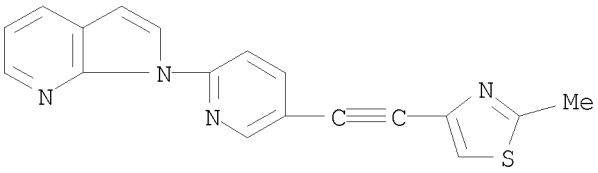
RN 935685-96-4 CAPLUS
CN Pyridine, 2-(2-chlorophenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



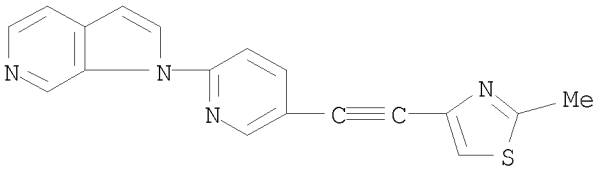
RN 935685-97-5 CAPLUS
CN Pyridine, 2-(2-methoxyphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



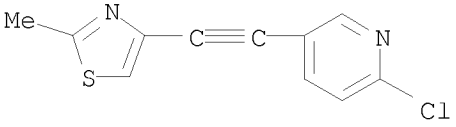
RN 935685-98-6 CAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 1-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]- (CA INDEX NAME)



RN 935686-20-7 CAPLUS
CN 1H-Pyrrolo[2,3-c]pyridine, 1-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl]- (CA INDEX NAME)



IT 329204-13-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of (thiazolylethynyl)pyridines and -pyrimidines as mGluR5 antagonists)
RN 329204-13-9 CAPLUS
CN Pyridine, 2-chloro-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



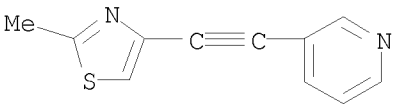
L4 ANSWER 15 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:344611 CAPLUS
DOCUMENT NUMBER: 147:681
TITLE: Predicting compound selectivity by self-organizing maps: cross-activities of metabotropic glutamate receptor antagonists
AUTHOR(S): Noeske, Tobias; Sasse, Britta C.; Stark, Holger; Parsons, Christopher G.; Weil, Tanja; Schneider,

Gisbert
CORPORATE SOURCE: Institute of Organic Chemistry and Chemical Biology ZAFES/CMP, Johann Wolfgang Goethe University, Frankfurt, 60323, Germany
SOURCE: ChemMedChem (2006), 1(10), 1066-1068
CODEN: CHEMGX; ISSN: 1860-7179
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A topol. pharmacophore descriptor (CATS) and self-organizing map (SOM)-based clustering were applied to predict potential activities of known metabotropic glutamate receptor (mGluR) antagonists. The tested compds. exhibited binding consts. in the micromolar range at predicted targets. The virtual screening concept is supposed to provide a basis for early recognition of potential side-effects in lead discovery.

IT 329205-68-7
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topol. pharmacophore descriptor (CATS) and self-organizing map (SOM)-based clustering to predict mGluR antagonists)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:332729 CAPLUS
DOCUMENT NUMBER: 146:358849
TITLE: Preparation of 1-({1-[(2-amino-6-methyl-4-pyridinyl)methyl]-4-fluoro-4-piperidinyl}carbonyl)-4-[2-(2-pyridinyl)-3H-imidazo[4,5-b]pyridin-3-yl]piperidine as histamine H3 receptor modulator
INVENTOR(S): De Lera Ruiz, Manuel; Aslanian, Robert G.; Berlin, Michael Y.; Mccormick, Kevin D.; Celly, Chander S.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 17pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070066644	A1	20070322	US 2006-523489	20060919
US 7332604	B2	20080219		
CA 2623025	A1	20070329	CA 2006-2623025	20060919
WO 2007035703	A1	20070329	WO 2006-US36424	20060919

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,

MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

EP 1931665	A1	20080618	EP 2006-803837		20060919
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US 20080058370	A1	20080306	US 2007-837248		20070810
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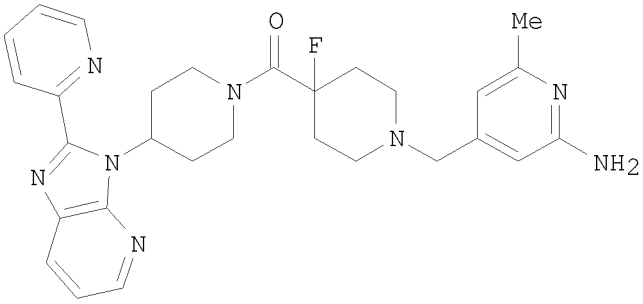
			US 2006-523489	A3	20060919
			WO 2006-US36424	W	20060919

GI



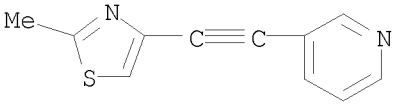
I

AB The present invention discloses the title compound I and pharmaceutically acceptable salts and solvates thereof. Synthesis of compound I, starting from Me 2-chloro-6-methylpyridine-4-carboxylate, was described. The invention also relates to pharmaceutical compns. comprising I and its use in treating obesity, metabolic syndrome, diabetes, hepatic lipidosis or nonalcoholic fatty liver disease. The invention also relates to the use of a combination of the compound I with addnl. therapeutic agents for treating obesity, metabolic syndrome, diabetes, hepatic lipidosis or nonalcoholic fatty liver disease.

IT 329205-68-7, 3-[(2-Methyl-1,3-thiazol-4-yl)ethynyl]pyridine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of 1-({1-[(2-amino-6-methyl-4-pyridinyl)methyl]-4-fluoro-4-piperidinyl}carbonyl)-4-[2-(2-pyridinyl)-3H-imidazo[4,5-b]pyridin-3-yl]piperidine as histamine H3 receptor modulator)

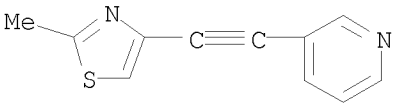
RN 329205-68-7 CAPLUS

CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:185376 CAPLUS
DOCUMENT NUMBER: 146:330636
TITLE: Comparison of the effects of mGluR1 and mGluR5 antagonists on the expression of behavioral sensitization to the locomotor effect of morphine and the morphine withdrawal jumping in mice
AUTHOR(S): Kotlinska, Jolanta; Bochenski, Marcin
CORPORATE SOURCE: Department of Pharmacology and Pharmacodynamics, Medical University, Lublin, 20-081, Pol.
SOURCE: European Journal of Pharmacology (2007), 558(1-3), 113-118
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of the present study was to compare the influence of group I metabotropic glutamate receptor (mGluR) antagonists (mGluR1 and mGluR5) on the expression of sensitization to the locomotor effect of morphine. We also tested how these compds. affect the morphine withdrawal jumps in mice. In our study, the mGluR1 antagonist EMQMCM [3-ethyl-2-methyl-quinolin-6-yl-(4-methoxy-cyclohexyl)-methanone methanesulfonate] and the mGluR5 antagonist MTEP ([(2-methyl-1,3-thiazol-4-yl) ethynyl] pyridine) were used. Sensitization was induced by five i.p. injections of morphine at the dose of 10 mg/kg, every 3 days. Morphine dependence was induced by s.c. implantation of pellets containing 37.5 mg of morphine base for three days. Our data indicate that pretreatment with EMQMCM (5, 10, 20 mg/kg) and MTEP (5, 10 mg/kg) on the challenge day, inhibited the expression of sensitization to the locomotor effect of morphine in mice. Antagonists of both subtypes of the group I mGlurs given alone, did not modify the acute locomotor effect of morphine. On the other hand, EMQMCM did not attenuate the morphine withdrawal jumps precipitated by naloxone (4 mg/kg). The results suggest that both subtypes of the group I mGluRs (mGluR1 and mGluR5) take part in the expression of morphine sensitization processes but mGluR1 is not involved in the expression of morphine withdrawal jumps in mice. These findings may have implications for the treatment of opiate addiction in future.
IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of effects of mGluR1 and mGluR5 antagonists on expression of behavioral sensitization to locomotor effect of morphine and morphine withdrawal jumps)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

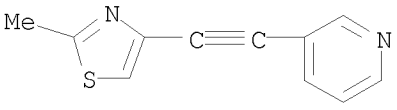
L4 ANSWER 18 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:171295 CAPLUS
DOCUMENT NUMBER: 146:493272
TITLE: The selective mGlu5 receptor antagonist MTEP, similar to NMDA receptor antagonists, induces social isolation in rats
AUTHOR(S): Koros, Eliza; Rosenbrock, Holger; Birk, Gerald; Weiss, Carmen; Sams-Dodd, Frank
CORPORATE SOURCE: Department of CNS Research, Boehringer-Ingelheim Pharma GmbH & Co. KG, Biberach, Germany
SOURCE: Neuropsychopharmacology (2007), 32(3), 562-576
CODEN: NEROEW; ISSN: 0893-133X
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has repeatedly been shown that uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonists can mimic certain aspects of pos. and neg. symptoms of schizophrenia in human volunteers and laboratory animals. The purpose of the present study was to expand these findings and to determine whether the selective metabotropic glutamate receptor subtype 5 (mGluR5) antagonist, MTEP (3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine), could induce similar effects in Wistar rats. First, MTEP (1.0-10.0 mg/kg; i.p.) after acute and subchronic (daily for 5 days) administration as well as the uncompetitive antagonists of the NMDA receptor of either high affinity, phencyclidine (0.5-4.0 mg/kg; s.c.) and (+)-MK-801 (0.03-0.25 mg/kg; s.c.), or low-moderate affinity, ketamine (2.0-16.0 mg/kg; s.c.) and memantine (0.15-20.0 mg/kg; s.c.), following daily administration for 3 days were tested in the social interaction test to determine their ability to reproduce the neg. and pos. symptoms measured by social isolation and stereotyped behavior, resp. Second, the compds. were tested in the motility test following acute administration to determine their ability to induce locomotor hyperactivity reflecting the pos. symptoms. In line with previous findings, all examined NMDA receptor antagonists produced social interaction deficits, locomotor hyperactivity, and stereotypy except memantine. Notably, this study found that MTEP following both acute and subchronic administration dose-dependently induced social isolation, but did not cause either locomotor hyperactivity or stereotypy. These data demonstrate that social behavior deficits in rats can be caused by both the blockade of the NMDA receptor and the inhibition of mGluR5, whereas mGluR5 antagonists may not independently be able to mimic the pos. symptoms.

IT 329205-68-7, 3-[(2-Methyl-1,3-thiazol-4-yl)ethynyl]pyridine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); BIOL (Biological study)
(3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine induced social isolation but did not cause locomotor hyperactivity and stereotypy in rat)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



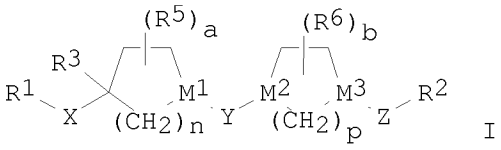
REFERENCE COUNT: 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 66 CAPLUS

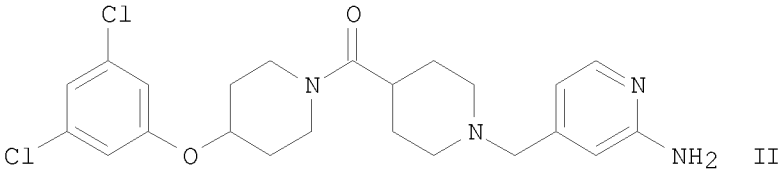
ACCESSION NUMBER: 2007:11886 CAPLUS
DOCUMENT NUMBER: 146:121827
TITLE: Piperidine derivatives useful as histamine H3 antagonists and their preparation, pharmaceutical compositions and use in the treatment of diseases
INVENTOR(S): Aslanian, Robert G.; Berlin, Michael Y.; Boyce, Christopher W.; Chao, Jianhua; De Lera Ruiz, Manuel; Mangiaracina, Pietro; McCormick, Kevin D.; Mutahi, Mwangi W.; Rosenblum, Stuart B.; Shih, Neng-Yang; Solomon, Daniel M.; Tom, Wing C.; Vaccaro, Henry A.; Zheng, Junying; Zhu, Xiaohong
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 119pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007001975	A1	20070104	WO 2006-US23800	20060619
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006262441	A1	20070104	AU 2006-262441	20060619
CA 2610959	A1	20070104	CA 2006-2610959	20060619
US 20070015807	A1	20070118	US 2006-455625	20060619
EP 1902046	A1	20080326	EP 2006-773528	20060619
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
MX 200800115	A	20080318	MX 2008-115	20071219
KR 2008021082	A	20080306	KR 2007-730855	20071228
PRIORITY APPLN. INFO.:			US 2005-692110P P	20050620
			WO 2006-US23800 W	20060619

OTHER SOURCE(S): MARPAT 146:121827
GI



I



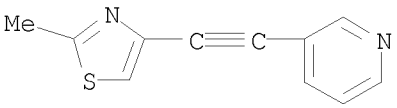
II

AB Disclosed are novel compds. of the formula I or a pharmaceutically acceptable salt thereof; compns. and methods of treating allergy-induced airway responses, congestions, obesity, metabolic syndrome, alc. fatty liver disease, hepatic steatosis, nonalcoholic steatohepatitis, cirrhosis, hepatacellular carcinoma and cognitive deficit disorders, using said compds., alone or in combination with other agents. Compds. of formula I wherein M1 and M3 are independently CH and N; M2 is CH, CF and N; Y is CO, CS, C1-5 alkyl, C-NOH and derivs., and SO1-2; X is NH and derivs., aminoalkyl, alkylamino, , C0-3 alkyl, etc.; Z is bond, (un)substituted C1-6 alkyl, (un)substituted alkoxy, (un)substituted alkylamino, etc.; R1 is H, (un)substituted alkyl, (un)substituted (hetero)cycloalkyl, (un)substituted (hetero)aryl, etc.; R2 is (un)substituted alkyl, (un)substituted alkenyl, (un)substituted (hetero)aryl, and (un)substituted (hetero)cycloalkyl; R3 is H, alkyl, (un)substituted (hetero)aryl, (un)substituted (hetero)cycloalkyl, and CONH2; R5 and R6 are independently halo, alkyl, OH, alkoxy, haloalkyl, CN, etc.; a and b are independently 0, 1 and 2; n and p are independently 1, 2 and 3; and their pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by etherification ot N-Boc-piperidin-4-ol with 3,5-dichlorophenol; the resulting N-Boc-4-(3,5-dichlorophenoxy) underwent hydrolysis to give 4-(3,5-dichlorophenoxy)piperidine, which underwent amidation with N-[2-(tert-butoxycarbonylamino)pyridin-4-ylmethyl]piperidine-4-carboxylic acid lithium salt; the resulting amide underwent hydrolysis to give compound II. All the invention compds. were evaluated for their histamine antagonistic activity (data given).

IT 329205-68-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of piperidine derivs. as histamine H3 antagonists useful in treatment of diseases)

RN 329205-68-7 CAPLUS

CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:11089 CAPLUS
DOCUMENT NUMBER: 146:93591
TITLE: Methods for treating neurological and psychiatric conditions, and test compound screening methods
INVENTOR(S): Haydon, Philip G.; Halassa, Michael M.; Fellin, Tommaso; Ding, Shinghua; Zhu, Yingzi
PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 89pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007002285	A2	20070104	WO 2006-US24303	20060621
WO 2007002285	A3	20071025		

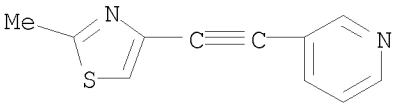
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2005-692513P P 20050621

AB The invention discloses methods for treating neurol. and psychiatric conditions. The methods comprise modulating the production or activity of one or more proteins that participate in calcium signaling or glutamate release in astrocytes, modulating the production or activity of one or more proteins that regulate the action of glial glutamate, modulating the concentration of calcium in the neuronal cell, modulating the expression or release of D-serine, or modulating the expression or release of ATP or adenosine. Methods to screen test compds. for their ability to target the specified pathways or cellular calcium are also disclosed.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for treating neurol. and psychiatric conditions, and test compound screening methods)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



L4 ANSWER 21 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1339718 CAPLUS
DOCUMENT NUMBER: 146:330473

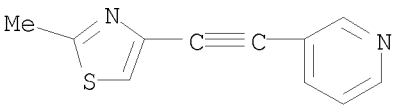
TITLE: Effect of the metabotropic glutamate 5 receptor antagonists MPEP and MTEP on the visceromotor response to colorectal distension in conscious rats
AUTHOR(S): Anon.
CORPORATE SOURCE: UK
SOURCE: Research Disclosure (2006), 511(Nov.), P1459-P1460 (No. 511020)
CODEN: RSDSBB; ISSN: 0374-4353
PUBLISHER: Kenneth Mason Publications Ltd.
DOCUMENT TYPE: Journal; Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RD 511020		20061110	RD 2006-511020	20061110

PRIORITY APPLN. INFO.: RD 2006-511020 20061110

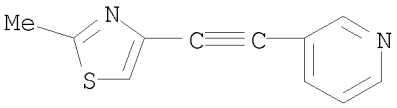
AB One of the leading theories concerning the pathogenesis of irritable bowel syndrome (IBS) is increased visceral sensitivity. Studies have shown that IBS patients have an altered rectal perception and that increased rectal pain is common in these patients during colorectal distension (CRD). CRD in animals and in man is a reliable and reproducible method to produce a visceral stimulus. In animals, visceral perception cannot be expressed verbally, which means various pseudo-affective responses to CRD in animals is termed the visceromotor response (VMR), which consists of contractions of the abdominal musculature. The amino acid glutamate is the primary excitatory transmitter in the mammalian central nervous system (CNS). It has been implicated that mGluR5 receptor antagonists can reduce visceral pain by acting both centrally and peripherally. Alterations in these pain pathways could be responsible for the visceral hypersensitivity present in IBS. The efficacy of various mGluR5 receptor antagonists on the VMR to isobaric CRD in rats is reported.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MTEP in dose-dependent manner inhibited visceromotor response to colorectal distension in conscious rat)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



L4 ANSWER 22 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1267239 CAPLUS
DOCUMENT NUMBER: 146:176960
TITLE: Neuroprotective activity of selective mGlu1 and mGlu5 antagonists in vitro and in vivo
AUTHOR(S): Szydlowska, Kinga; Kaminska, Bozena; Baude, Andrea; Parsons, Chris G.; Danysz, Wojciech
CORPORATE SOURCE: Laboratory of Transcription Regulation, The Nencki Institute of Experimental Biology, Warsaw, 02-093, Pol.
SOURCE: European Journal of Pharmacology (2007), 554(1), 18-29

CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The neuroprotective potential of allosteric mGlu5 and mGlu1 antagonists such as MPEP, MTEP, and EMQMCM, was tested in vitro in organotypic hippocampal cultures and in the middle cerebral artery occlusion model of stroke in vivo. Both classes of agent have high selectivity toward mGlu sub-types and are active in animal models of various diseases indicating satisfactory CNS penetration. In organotypic hippocampal cultures MPEP showed high neuroprotective potency against sub-chronic (12 days) insult produced by 3-NP with an IC50 of c.a. 70 nM. In contrast, although the mGlu1 antagonist EMQMCM was also protective, it seems to be weaker yielding an IC50 of c.a. 1 μM. Similarly, in the transient (90 min) middle cerebral artery occlusion model of ischemia in rats, MTEP seems to be more effective than EMQMCM. MTEP, at 2.5 mg/kg and at 5 mg/kg provided 50 and 70% neuroprotection if injected 2 h after the onset of ischemia. At a dose of 5 mg/kg, significant (50%) neuroprotection was also seen if the treatment was delayed by 4 h. EMQMCM was not protective at 5 mg/kg (given 2 h after occlusion) but at 10 mg/kg 50% of neuroprotection was observed The present data support stronger neuroprotective potential of mGlu5 than mGlu1 antagonists.
IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotective activity of selective mGlu1 and mGlu5 antagonists in vitro and in vivo)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



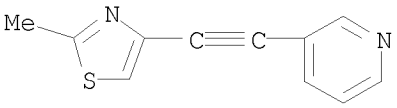
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1239249 CAPLUS
DOCUMENT NUMBER: 146:135320
TITLE: Antidepressant-like effects of mGluR1 and mGluR5 antagonists in the rat forced swim and the mouse tail suspension tests
AUTHOR(S): Belozertseva, I. V.; Kos, T.; Popik, P.; Danysz, W.; Bespalov, A. Y.
CORPORATE SOURCE: Institute of Pharmacology, Pavlov Medical University, St. Petersburg, 197089, Russia
SOURCE: European Neuropsychopharmacology (2007), 17(3), 172-179
CODEN: EURNE8; ISSN: 0924-977X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Drugs that act to reduce glutamatergic neurotransmission such as NMDA receptor antagonists exert antidepressant-like effects in a variety of exptl. paradigms, but their therapeutic application is limited by undesired side effects. In contrast, agents that reduce glutamatergic

tone by blocking type I metabotropic glutamate receptors have been suggested to have more a favorable side-effect profile. The present study aimed to compare the effects of mGluR1 antagonist (EMQMCM; JNJ16567083, 3-ethyl-2-methyl-quinolin-6-yl)-(4-methoxy-cyclohexyl)-methanone methanesulfonate, 0.156-10 mg/kg) and mGluR5 antagonist (MTEP, [(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine, 1.25-10 mg/kg) in two behavioral screening assays commonly used to assess antidepressant-like activity. In the modified forced swim test in rats, imipramine (used as a pos. control) decreased immobility (MED 40 mg/kg) and increased the duration of escape-oriented (climbing and diving; MED 20 mg/kg) behaviors. Both EMQMCM and MTEP decreased the floating duration (MED 1.25 and 2.5 mg/kg) and increased the duration of mobile behaviors (paddling and swimming; MED 2.5 and 5 mg/kg). EMQMCM but not MTEP increased the duration of escape behaviors (climbing and diving; MED 1.25 mg/kg). In the mouse tail suspension test, EMQMCM (5 but not 2.5, 10 and 25 mg/kg), 2-methyl-6-(phenylethynyl)-pyridine (MPEP, 10 but not 1 mg/kg) and MTEP (MED 25 mg/kg) decreased immobility scores. For EMQMCM, the dose-effect relationship was biphasic. With the exception of EMQMCM (10 mg/kg), locomotor activity in mice was not affected by treatments. The present study therefore suggests that acute blockade of mGluR5 and also of mGluR1 exerts antidepressant-like effects in behavioral despair tests in rats and mice.

IT 329205-68-7, MTEP
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antidepressant effects of mGluR1 and mGluR5 antagonists in drug screening assays: rat forced swim and mouse tail suspension tests)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

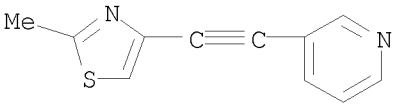
L4 ANSWER 24 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1205530 CAPLUS
DOCUMENT NUMBER: 146:19224
TITLE: Are compounds acting at metabotropic glutamate receptors the answer to treating depression?
AUTHOR(S): Palucha, Agnieszka
CORPORATE SOURCE: Institute of Pharmacology, Polish Academy of Sciences, Krakow, 31343, Pol.
SOURCE: Expert Opinion on Investigational Drugs (2006), 15(12), 1545-1553
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Numerous studies over the last few years have suggested that modulating the glutamatergic system may be an efficient method to achieve an antidepressant effect. Data suggest that metabotropic glutamate receptors (mGlu receptors), related to long-term, modulatory effects on glutamatergic neurotransmission, may be a good target for the development of new, effective and safe therapeutic drugs to treat several CNS

disorders including depression and anxiety. Several potent, selective and systemically active orthosteric and allosteric ligands of specific mGlu receptor subtypes have been discovered and these have been tested as potential antidepressants in models of depression in rodents. The mGluR5 antagonists and group II mGlu receptor antagonists seem to be the most promising compds. with potential antidepressant-like activity; however, the efficacy of mGlu receptor ligands in the clin. setting is still an unanswered question.

IT 329205-68-7, MTEP
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabotropic glutamate receptors antagonists with potential antidepressant-like activity)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

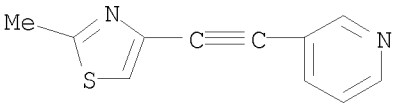
L4 ANSWER 25 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1047237 CAPLUS
DOCUMENT NUMBER: 145:348469
TITLE: Metabotropic glutamate 5 receptor antagonism is associated with antidepressant-like effects in mice
AUTHOR(S): Li, Xia; Need, Anne B.; Baez, Melvyn; Witkin, Jeffrey M.
CORPORATE SOURCE: Neuroscience Discovery Research, Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2006), 319(1), 254-259
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Antidepressant-like effects of metabotropic glutamate (mGlu)5 receptor antagonists have been reported previously. We now provide definitive identification of mGlu5 receptors as a target for these effects through the combined use of selective antagonists and mice with targeted deletion of the mGlu5 protein. In these expts., the mGlu5 receptor antagonists 2-methyl-6-(phenylethynyl)-pyridine (MPEP) and the more selective and metabolically stable analog 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]-pyridine (MTEP) decreased immobility in the mouse forced swim test, a test predictive of antidepressant efficacy in humans. MGlu5 receptor knockout mice had a phenotype in the forced swim test that was congruent with the effects of receptor blockade; mGlu5 receptor knockout mice were significantly less immobile than their wild-type counterparts. Consistent with mGlu5 receptor mediation of the antidepressant-like effects of MPEP, the effects of MPEP were not observed in mGlu5 receptor knockout mice, whereas comparable effects of the tricyclic antidepressant imipramine remained active in the mutant mice. MPEP and imipramine resulted in a synergistic antidepressant-like effect in the forced swim test. The drug interaction was not likely because of increased levels of drugs in the

brain, suggesting a pharmacodynamic interaction of mGlu5 and monoaminergic systems in this effect. Thus, the present findings substantiate the hypothesis that mGlu5 receptor antagonism is associated with antidepressant-like effects. This mechanism may not only provide a novel approach to the therapeutic management of depressive disorders but also may be useful in the augmentation of effects of traditional antidepressant agents.

IT 329205-68-7, MTEP
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabotropic glutamate 5 receptor antagonism is associated with antidepressant-like effects in mice)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



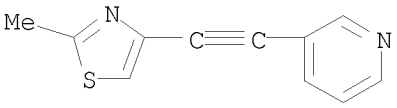
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:983183 CAPLUS
DOCUMENT NUMBER: 146:433746
TITLE: Metabotropic glutamate receptor subtype 5 antagonists MPEP and MTEP
AUTHOR(S): Lea, Paul M., IV; Faden, Alan I.
CORPORATE SOURCE: New Health Sciences Inc., Bethesda, MD, USA
SOURCE: CNS Drug Reviews (2006), 12(2), 149-166
CODEN: CDREFB; ISSN: 1080-563X
PUBLISHER: Blackwell Publishing, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Glutamate regulates the Sanction of central nervous system (CNS), in part, through the cAMP and/or IP3/DAG second messenger-associated metabotropic glutamate receptors (mGluRs). The mGluR5 antagonist 2-methyl-6-(phenylethynyl)-pyridine (MPEP) has been extensively used to elucidate potential physiol. and pathophysiol. functions of mGluR5. Unfortunately, recent evidence indicates significant non-specific actions of MPEP, including inhibition of NMDA receptors. In contrast, in vivo and in vitro characterization of the newer mGluR5 antagonist 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (MTEP) indicates that it is more highly selective for mGluR5 over mGluR1, has no effect on other mGluR subtypes, and has fewer off-target effects than MPEP. This article reviews literature on both of these mGluR5 antagonists, which suggests their possible utility in neurodegeneration, addiction, anxiety and pain management.

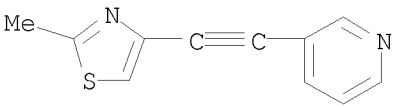
IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine is more specific metabotropic glutamate receptor subtype 5 antagonist than MPEP, suggesting MTEP can be used in management of neurodegeneration, addiction, anxiety and pain)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



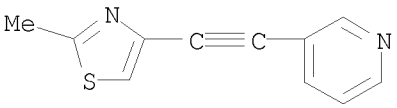
REFERENCE COUNT: 218 THERE ARE 218 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:967564 CAPLUS
DOCUMENT NUMBER: 145:499939
TITLE: A combined marble burying-locomotor activity test in mice: A practical screening test with sensitivity to different classes of anxiolytics and antidepressants
AUTHOR(S): Nicolas, Laurent B.; Kolb, Yeter; Prinssen, Eric P. M.
CORPORATE SOURCE: CNS Research, F. Hoffmann-La Roche Ltd., Basel, CH-4070, Switz.
SOURCE: European Journal of Pharmacology (2006), 547(1-3), 106-115
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Over the last decades, the inhibition of spontaneous burying of glass marbles by mice has been used as an index of anxiolytic drug action in the so-called marble burying test. Indeed, acute administration of rapid-onset (e.g. diazepam) and slow-onset (e.g. fluoxetine) anxiolytics inhibit marble burying. However, non-anxiolytic compds. such as classical antipsychotics also reduce marble burying thus suggesting that the predictive validity of this procedure for anxiety may be limited. In the present study, after having selected a strain of mice (C57BL/6J) that showed spontaneous avoidance of glass marbles, we tried to improve the predictive validity of the marble burying test for anxiety by measuring locomotor activity during the marble burying test and - if needed - in control expts. by using a videotracking system. Twenty-four reference compds. were tested including anxiolytics, anxiogenics, antidepressants, antipsychotics and other classes. By comparing marble burying scores with locomotor measures, we found that, based on our criteria, most of the anxiolytics and antidepressants selectively inhibited marble burying in contrast to most of the other compds. (e.g. haloperidol, morphine). Two putative anxiolytics, i.e. the nociceptin orphanin FQ peptide receptor agonist Ro 64-6198 and the metabotropic glutamate 5 receptor antagonist 2-methyl-6-(phenylethynyl)pyridine, also showed a selective profile. We propose this modified procedure, requiring only a limited number of animals, as a valuable screening test for the detection of compds. having anxiolytic effects.
IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined marble burying-locomotor activity screening test in mice with sensitivity to different classes of anxiolytics and antidepressants)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



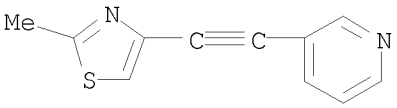
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:962695 CAPLUS
DOCUMENT NUMBER: 145:465173
TITLE: Recursive Partitioning for the Prediction of Cytochromes P450 2D6 and 1A2 Inhibition: Importance of the Quality of the Dataset
AUTHOR(S): Burton, Julien; Ijjaali, Ismail; Barberan, Olivier; Petitet, Francois; Vercauteren, Daniel P.; Michel, Andre
CORPORATE SOURCE: Laboratoire de Physico-Chimie Informatique, Facultes Universitaires Notre-Dame de la Paix, Namur, B-5000, Belg.
SOURCE: Journal of Medicinal Chemistry (2006), 49(21), 6231-6240
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to explore the use of detailed biol. data in combination with a statistical learning method for predicting the CYP1A2 and CYP2D6 inhibition. Data were extracted from the Aureus-Pharma highly structured databases which contain precise measures and detailed exptl. protocol concerning the inhibition of the two cytochromes. The methodol. used was Recursive Partitioning, an easy and quick method to implement. The building of models was preceded by the evaluation of the chemical space covered by the datasets. The descriptors used are available in the MOE software suite. The models reached at least 80% of Accuracy and often exceeded this percentage for the Sensitivity (Recall), Specificity, and Precision parameters. CYP2D6 datasets provided 11 models with Accuracy over 80%, while CYP1A2 datasets counted 5 high-accuracy models. Our models can be useful to predict the ADME properties during the drug discovery process and are indicated for high-throughput screening.
IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Recursive Partitioning for prediction of cytochromes P 450 2D6 and 1A2 inhibition: importance of quality of dataset)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:914190 CAPLUS
DOCUMENT NUMBER: 145:328210
TITLE: Estrus variation in anticonflict-like effects of the mGlu5 receptor antagonist MTEP, microinjected into lateral septal nuclei of female Wistar rats
AUTHOR(S): Molina-Hernandez, M.; Tellez-Alcantara, N. P.; Perez-Garcia, J.; Olivera-Lopez, J. I.; Jaramillo, M. Teresa
CORPORATE SOURCE: Laboratorio de Conducta, Instituto de Investigaciones Psicologicas, Universidad Veracruzana, Veracruz, Mex.
SOURCE: Pharmacology, Biochemistry and Behavior (2006), 84(3), 385-391
CODEN: PBBHAU; ISSN: 0091-3057
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Anticonflict-like effects of the mGlu5 receptor antagonist MTEP (systemic administrations: 1.50, 3.0 or 6.0 mg/kg; i.p.; intra-lateral septal nuclei or intra-medial septal region infusions: 2.5 μg/μl, 5.0 μg/μl or 10.0 μg/μl) were assessed in Wistar rats during late proestrus or metestrus-diestrus. Results showed that control rats displayed an increased number of immediately punished reinforcers during late proestrus ($P < 0.05$), when compared to metestrus-diestrus. During late proestrus, systemic administrations (3.0 mg/kg, $P < 0.05$; 6.0 mg/kg $P < 0.05$) or intra-lateral septal nuclei infusions (5.0 μg/μl, $P < 0.05$; 10.0 μg/μl, $P < 0.05$) of MTEP increased the number of immediately punished reinforcers received. During metestrus-diestrus only the highest doses of MTEP (systemic administration: 6.0 mg/kg $P < 0.05$; intra-lateral septal nuclei infusions: 10.0 μg/μl, $P < 0.05$) increased the number of immediately punished reinforcers obtained. MTEP infusions into the medial septum produced neither of these anticonflict effects. In conclusion, data showed an estrus variation in those anticonflict-like effects of the mGlu5 receptor antagonist MTEP, systemically administered or microinjected into lateral septal nuclei of female Wistar rats.
IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrus variation in anticonflict-like effects of the mGlu5 receptor antagonist MTEP, microinjected into lateral septal nuclei of female Wistar rats)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



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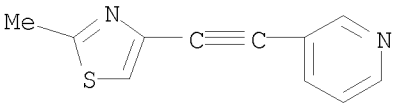
L4 ANSWER 30 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:837063 CAPLUS
DOCUMENT NUMBER: 145:432066
TITLE: Analgesic effects of mGlu1 and mGlu5 receptor antagonists in the rat formalin test
AUTHOR(S): Sevostianova, N.; Danysz, W.

CORPORATE SOURCE: Merz Pharmaceuticals GmbH, Frankfurt/Main, 60318, Germany
SOURCE: Neuropharmacology (2006), 51(3), 623-630
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB MGlu1 and mGlu5 receptors have been implicated in pain associated with inflammation. In the present study, the formalin test was used to measure sustained pain with components of tissue injury. The aims of the present study were to assess: (i) the role of mGlu1 and mGlu5 receptors in inflammatory pain using selective antagonist EMQMCM, 1.25-5 mg/kg, as the mGlu1 receptor antagonist, and MPEP or MTEP, 2.5-10 mg/kg, as mGlu5 receptor antagonist; (ii) the possible interaction between mGlu1 and mGlu5 receptor antagonists and morphine; and (iii) whether tolerance develops to the analgesic effects of these antagonists after prolonged treatment. EMQMCM, MTEP and MPEP significantly reduced the manifestation of both phases of formalin response. However, all these mGlu receptor antagonists did not affect the withdrawal latencies in a model of acute pain (Hargreaves test), which has a different underlying mechanism. In the present study, the suppressive effect on formalin-induced pain behavior was much stronger when mGlu1 and mGlu5 receptor antagonists were co-injected compared to administration of a single antagonist, but this effect was not seen when mGlu receptor antagonist was co-administered with morphine. This is in contrast to the pronounced inhibitory effects after co-treatment with morphine and the uncompetitive NMDA receptor antagonist memantine. The present study also provides the first direct in vivo evidence that prolonged administration of MTEP (5 mg/kg) over 7 days leads to the development of tolerance to its antinociceptive effects. Such tolerance was not observed when EMQMCM (5 mg/kg) was administered in the same manner. In conclusion, these results provide addnl. arguments for the role of group I mGlu receptors in pain with inflammatory conditions.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesic effects of mGlu1 and mGlu5 receptor antagonists in rat formalin test)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:788503 CAPLUS
DOCUMENT NUMBER: 145:328200

TITLE: Effects of group I metabotropic glutamate receptor antagonists on the behavioral sensitization to motor effects of cocaine in rats

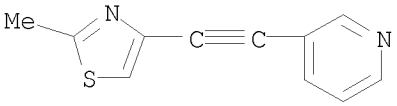
AUTHOR(S): Dravolina, Olga A.; Danysz, Wojciech; Bespalov, Anton Y.
CORPORATE SOURCE: Laboratory of Behavioral Pharmacology, Institute of Pharmacology, Pavlov Medical University, St.

Petersburg, 197089, Russia
SOURCE: Psychopharmacology (Berlin, Germany) (2006), 187(4), 397-404
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Rationale: Metabotropic glutamate receptors (mGluRs) were reported to regulate various behavioral effects of addictive drugs. Objective: The present study evaluated the role of group I mGluRs in the progressive augmentation ("sensitization") of the behavioral effects observed after repeated, intermittent cocaine exposure. Materials and methods: After habituation to handling and baseline activity measurement (days 1-2), rats received eight injections of cocaine (10 mg/kg) or saline on days 3-6, 8-11, and then, were tested twice with acute saline and cocaine given in a counterbalanced manner on days 13 and 15. Before the test sessions, subjects were pretreated with mGluR1 antagonist EMQMCM (JNJ16567083, (3-ethyl-2-methyl-quinolin-6-yl)-(4-methoxy-cyclohexyl)-methanone methanesulfonate) and mGluR5 antagonist MTEP ([(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine). Results: Pretreatment with EMQMCM (2.5-10 mg/kg) but not MTEP (2.5-10 mg/kg) significantly reduced expression of the sensitized ambulatory motor activity of the cocaine-experienced animals acutely challenged with cocaine. Both EMQMCM and MTEP significantly reduced vertical motor activity across all cocaine/saline treatment conditions. Conclusions: These findings indicate that the expression of behavioral sensitization to cocaine-induced stimulation of locomotor activity may be modulated by group I mGluR antagonists (mGluR1 rather than mGluR5), but these effects occur at the dose levels that attenuate vertical activity.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of group I metabotropic glutamate receptor antagonists on behavioral sensitization to motor effects of cocaine in rats)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

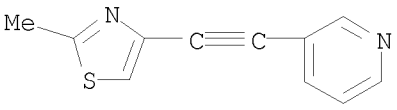
L4 ANSWER 32 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:635588 CAPLUS
DOCUMENT NUMBER: 146:19990
TITLE: Antidepressant-like and anxiolytic-like actions of the mGlu5 receptor antagonist MTEP, microinjected into lateral septal nuclei of male Wistar rats
AUTHOR(S): Molina-Hernandez, Miguel; Tellez-Alcantara, Norma Patricia; Perez-Garcia, Julian; Olivera-Lopez, Jorge Ivan; Jaramillo, M. Teresa
CORPORATE SOURCE: Laboratorio de Psicobiologia y Etologia, Instituto de Investigaciones Psicologicas, Universidad Veracruzana, Veracruz, Mex.
SOURCE: Progress in Neuro-Psychopharmacology & Biological

Psychiatry (2006), 30(6), 1129-1135
CODEN: PNPPD7; ISSN: 0278-5846
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study describes the effects of intra-lateral septal infusions of different doses of the mGluR5 antagonist MTEP in the DRL-72 s paradigm and the elevated plus-maze test in rats, two behavioral models known to be sensitive to antidepressant-like and anxiolytic-like drug effects, resp. Intra-lateral septal infusions of MTEP induced a dose-dependent (5.0 μg/μl, P < 0.05; 10.0 μg/μl, P < 0.05) increase in reinforced lever presses and a cohesive rightward shift of the inter-response time distribution (5.0 μg/μl, P < 0.05; 10.0 μg/μl, P < 0.05). These effects are indicative of antidepressant-like actions of the compound Desipramine, a prototypical antidepressant drug, induced (5.0 μg/μl; P < 0.05) similar effects. In the elevated plus-maze test, intra-lateral septal infusions of MTEP (5.0 μg/μl, P < 0.05; 10.0 μg/μl, P < 0.05) increased the exploration of the open arms without affecting locomotion. This anxiolytic-like effect was similar to that observed with the infusion of the benzodiazepine midazolam (10.0 μg/μl; P < 0.05) in the same brain area. It is concluded that intra-lateral septal infusions of the mGlu5 receptor antagonist MTEP produced antidepressant-like actions or anxiolytic-like effects in male rats.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intra-lateral septal infusions of mGlu5 receptor antagonist MTEP into lateral septal nuclei produce antidepressant-like actions or anxiolytic-like effects in male rat)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



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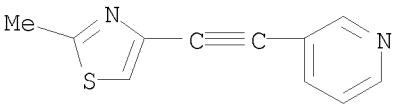
L4 ANSWER 33 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:536861 CAPLUS
DOCUMENT NUMBER: 145:284863
TITLE: mGlu1 and mGlu5 receptor antagonists lack anticonvulsant efficacy in rodent models of difficult-to-treat partial epilepsy
AUTHOR(S): Loescher, Wolfgang; Dekundy, Andrzej; Nagel, Jens; Danysz, Wojciech; Parsons, Chris G.; Potschka, Heidrun
CORPORATE SOURCE: Department of Pharmacology, Toxicology and Pharmacy, University of Veterinary Medicine, Hannover, D-30559, Germany
SOURCE: Neuropharmacology (2006), 50(8), 1006-1015
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Modulation of metabotropic glutamate (mGlu) receptors represents an interesting new approach for the treatment of a range of neurol. and

psychiatric disorders. Several lines of evidence suggest that functional blockade of group I (mGlu1 and mGlu5) receptors may be beneficial for treatment of epileptic seizures. This study was conducted to investigate whether mGlu1 or mGlu5 receptor antagonists have the potential to block partial or secondarily generalized seizures as occurring in partial epilepsy, the most common and difficult-to-treat type of epilepsy in patients. For this purpose, we systemically administered novel highly selective and brain penetrable group I mGlu receptor antagonists, i.e., the mGlu1 receptor antagonist EMQMCM [3-ethyl-2-methyl-quinolin-6-yl-(4-methoxy-cyclohexyl)-methanone methanesulfonate] and the mGlu5 receptor antagonist MTEP ([(2-methyl-1,3-thiazol-4-yl) ethynyl] pyridine), at doses appropriate for mGlu1 or mGlu5 receptor-mediated effects in rodent models of partial seizures. Two models were used: The 6-Hz electroshock model of partial seizures in mice and the amygdala-kindling model in rats. Clin. established antiepileptic drugs were included in the expts. for comparison. Antiepileptic drugs exerted significant anticonvulsant effects in both models, while EMQMCM and MTEP were ineffective in this regard, although both compds. were administered up to doses associated with essentially full receptor occupancy and with typical mGlu receptor-mediated effects in rodent models of anxiety or pain. Brain microdialysis for determining extracellular levels of MTEP following i.p. administration in rats substantiated that effective brain concns. were reached at times of our expts. in seizure models. The present results do not support a significant anticonvulsant potential of group I mGlu receptor antagonists in rodent models of difficult-to-treat partial epilepsy.

IT 329205-68-7, MTEP
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mGlu1 and mGlu5 receptor antagonists lack anticonvulsant efficacy in rodent models of difficult-to-treat partial epilepsy)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



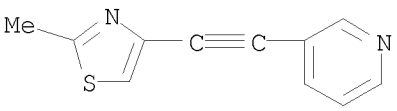
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 34 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:314835 CAPLUS
DOCUMENT NUMBER: 144:480888
TITLE: Neuroprotective potential of group I metabotropic glutamate receptor antagonists in two ischemic models
AUTHOR(S): Makarewicz, Dorota; Duszczyk, Malgorzata; Gadamski, Roman; Danysz, Wojciech; Lazarewicz, Jerzy W.
CORPORATE SOURCE: Department of Neurochemistry, Medical Research Centre, Polish Academy of Sciences, Warsaw, 02-106, Pol.
SOURCE: Neurochemistry International (2006), 48(6-7), 485-490
CODEN: NEUIDS; ISSN: 0197-0186
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The neuroprotective potential of mGluR1 and mGluR5 antagonists (group I),

EMQMCM and MTEP, resp. was studied using the 3 min forebrain ischemia model in Mongolian gerbils and the hypoxia-ischemia model in 7-day-old rats. Hypoxia-ischemia was induced by unilateral carotid occlusion followed by 75 min exposure to hypoxia (7.3% O2 in N2), forebrain ischemia in gerbils was evoked by bilateral common carotid artery occlusion. The postischemic rectal body temperature in rat pups or brain temperature of gerbils was measured. The drugs were administered i.p. three times every 2 h after the insult, each time in equal doses of 1.25, 2.5 or 5.0 mg/kg. After 2 wk brain damage was evaluated as weight decrease of the ipsilateral hemisphere in the rat pups or damage to CA1 pyramids in the gerbil hippocampus. The results demonstrated a dose dependent neuroprotection in both ischemic models by EMQMCM, while MTEP was neuroprotective only in the gerbil model of forebrain ischemia. EMQMCM reduced postischemic hyperthermia in gerbils. Thus, the antagonists of mGluR1 and mGluR5 show differential neuroprotective ability in two models of brain ischemia. Postischemic hypothermia may be partially involved in the mechanism of neuroprotection following EMQMCM in gerbils.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotective potential of group I metabotropic glutamate receptor antagonists in two ischemic models)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

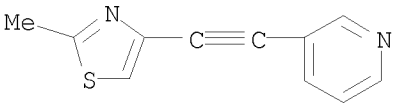
L4 ANSWER 35 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:314834 CAPLUS
DOCUMENT NUMBER: 145:180745
TITLE: Antagonists of group I metabotropic glutamate receptors do not inhibit induction of ischemic tolerance in gerbil hippocampus
AUTHOR(S): Duszczyk, Malgorzata; Gadamski, Roman; Ziembowicz, Apolonia; Lazarewicz, Jerzy W.
CORPORATE SOURCE: Department of Neurochemistry, Medical Research Centre, Polish Academy of Sciences, Warsaw, 02-106, Pol.
SOURCE: Neurochemistry International (2006), 48(6-7), 478-484
CODEN: NEUIDS; ISSN: 0197-0186
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this study we tested the effect of antagonists of 2 subtypes of the group I metabotropic glutamate receptors (mGluRs GI) on the induction of ischemic tolerance in relation to brain temperature These expts. were prompted by indications that glutamate receptors may participate in the mechanisms of ischemic preconditioning. The role of NMDA receptors in the induction of ischemic tolerance was debated while there is lack of information concerning the involvement of mGluRs GI in this phenomenon. The tolerance to injurious 3 min forebrain ischemia in Mongolian gerbils was induced 48 h earlier by 2 min preconditioning ischemia. Brain temperature was measured

using telemetry equipment. EMQMCM and MTEP, antagonists of mGluR1 and mGluR5, resp., were injected i.p. at a dose of 5 mg/kg. They were administered either before preconditioning ischemia in a single dose or after 2 min ischemia three times every 2 h. Both antagonists did not inhibit the induction of ischemic tolerance. Thus, our data indicate that group I metabotropic glutamate receptors do not play an essential role in the induction of ischemic tolerance.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(group I metabotropic glutamate receptor antagonists do not inhibit induction of ischemic tolerance in gerbil hippocampus)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

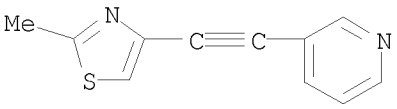
L4 ANSWER 36 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:287053 CAPLUS
DOCUMENT NUMBER: 145:284774
TITLE: Effects of group I metabotropic glutamate receptors blockade in experimental models of Parkinson's disease
AUTHOR(S): Dekundy, Andrzej; Pietraszek, Malgorzata; Schaefer, Daniela; Cenci, M. Angela; Danysz, Wojciech
CORPORATE SOURCE: Preclinical R&D, Merz Pharmaceuticals GmbH, Frankfurt am Main, 60318, Germany
SOURCE: Brain Research Bulletin (2006), 69(3), 318-326
CODEN: BRBUDU; ISSN: 0361-9230
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study was devoted to investigate the effects of the metabotropic glutamate receptor(mGluR)5 antagonist [(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (MTEP) and the mGluR1 antagonist, (3-ethyl-2-methyl-quinolin-6-yl)-(4-methoxy-cyclohexyl)-methanone methanesulfonate (EMQMCM), in animal studies indicative of antiparkinsonian-like activity such as haloperidol-induced catalepsy, hypoactivity in open field following haloperidol, and rotation in rats with unilateral 6-hydroxydopamine(OHDA)-induced lesions of the midbrain dopaminergic system (alone and in combination with -DOPA). Moreover, antidyskinetic activity of different mGluR ligands was evaluated in the rat model of -DOPA-induced dyskinesia. Both MTEP (5 mg/kg) and EMQMCM (4 mg/kg) slightly inhibited haloperidol (0.5 mg/kg)-induced catalepsy. However, neither substance reversed the hypoactivity produced by haloperidol (0.2 mg/kg). Although MTEP did not produce significant turning, it inhibited contralateral rotations after -DOPA (at 5 mg/kg) and alleviated -DOPA-induced dyskinesia (at 2.5 and 5 mg/kg) in 6-OHDA-lesioned rats. In contrast, mGluR1 antagonists EMQMCM and RS-1-aminoindan-1,5-dicarboxylic acid (AIDA) failed to modify -DOPA-induced dyskinesia. The results of the present study suggest that either subtype of group I of mGluRs may be involved in the pathol. altered circuitry in the basal ganglia. However, the equivocal results do not

strongly support the hypothesis that mGluR1 and mGluR5 antagonists may be beneficial in the symptomatic treatment of Parkinson's disease. However, mGluR5 antagonists may prove useful for the symptomatic treatment of -DOPA-induced dyskinesia.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
([(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine slightly inhibited haloperidol-induced catalepsy did not reverse haloperidol induced hypoactivity but reversed L-DOPA-induced rotation and dyskinesia in rat model of Parkinson's disease)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

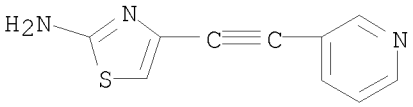
L4 ANSWER 37 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:20956 CAPLUS
DOCUMENT NUMBER: 144:274179
TITLE: Synthesis and Structure-Activity Relationships of 3-[(2-Methyl-1,3-thiazol-4-yl)ethynyl]pyridine Analogues as Potent, Noncompetitive Metabotropic Glutamate Receptor Subtype 5 Antagonists; Search for Cocaine Medications
AUTHOR(S): Iso, Yasuyoshi; Grajkowska, Ewa; Wroblewski, Jarda T.; Davis, Jared; Goeders, Nicholas E.; Johnson, Kenneth M.; Sanker, Subramaniam; Roth, Bryan L.; Tueckmantel, Werner; Kozikowski, Alan P.
CORPORATE SOURCE: Drug Discovery Program, Department of Medicinal Chemistry and Pharmacognosy, University of Illinois at Chicago, Chicago, IL, 60612, USA
SOURCE: Journal of Medicinal Chemistry (2006), 49(3), 1080-1100
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:274179

AB Recent genetic and pharmacol. studies have suggested that the metabotropic glutamate receptor subtype 5 (mGluR5) may represent a druggable target in identifying new therapeutics for the treatment of various central nervous system disorders including drug abuse. In particular, considerable attention in the mGluR5 field has been devoted to identifying ligands that bind to the allosteric modulatory site, distinct from the site for the primary agonist glutamate. Both 2-methyl-6-(phenylethynyl)pyridine (MPEP) and its analog 3-[(2-methyl-4-thiazolyl)ethynyl]pyridine (MTEP) have been shown to be selective and potent noncompetitive antagonists of mGluR5. Because of results presented in this study showing that MTEP prevents the reinstatement of cocaine self-administration caused by the presentation of environmental cues previously associated with cocaine availability, a series of analogs of MTEP was prepared with the aim of gaining a better understanding of the structural features relevant to its antagonist

potency and with the ultimate aim of investigating the effects of such compds. in blunting the self-administration of cocaine. These efforts have led to the identification of compds. showing higher potency as mGluR5 antagonists than either MPEP or MTEP. Two compds. exhibited functional activity as mGluR5 antagonists that are 490 and 230 times, resp., better than that of MTEP.

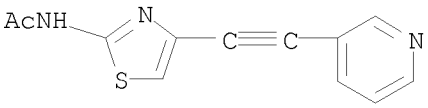
IT 329205-54-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino[(pyridinyl)ethynyl]thiazole derivs. and study of their activity as noncompetitive metabotropic glutamate receptor subtype-5 (mGluR5) antagonists)

RN 329205-54-1 CAPLUS
CN 2-Thiazolamine, 4-[2-(3-pyridinyl)ethynyl]- (CA INDEX NAME)

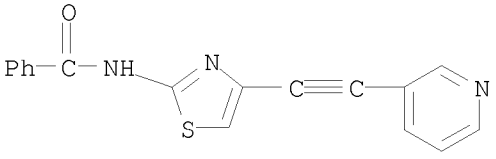


IT 878018-66-7P 878018-68-9P 878018-70-3P
878018-72-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of amino[(pyridinyl)ethynyl]thiazole derivs. and study of their activity as noncompetitive metabotropic glutamate receptor subtype-5 (mGluR5) antagonists)

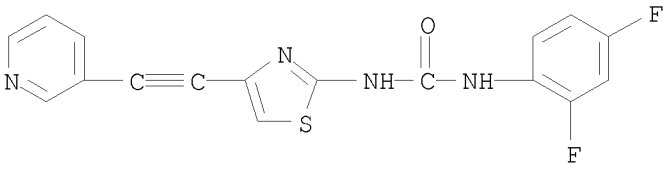
RN 878018-66-7 CAPLUS
CN Acetamide, N-[4-[2-(3-pyridinyl)ethynyl]-2-thiazolyl]- (CA INDEX NAME)



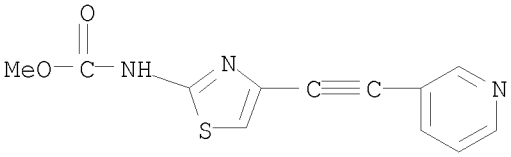
RN 878018-68-9 CAPLUS
CN Benzamide, N-[4-[2-(3-pyridinyl)ethynyl]-2-thiazolyl]- (CA INDEX NAME)



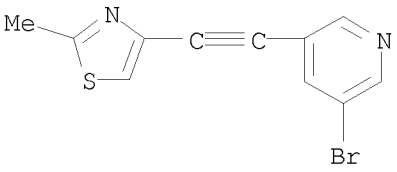
RN 878018-70-3 CAPLUS
CN Urea, N-(2,4-difluorophenyl)-N'-[4-[2-(3-pyridinyl)ethynyl]-2-thiazolyl]- (CA INDEX NAME)



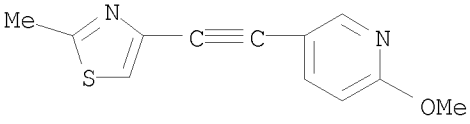
RN 878018-72-5 CAPLUS
CN Carbamic acid, [4-(3-pyridinylethynyl)-2-thiazolyl]-, methyl ester (9CI) (CA INDEX NAME)



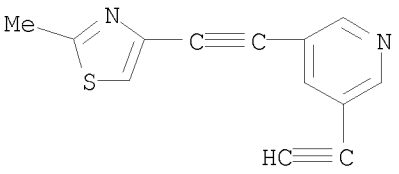
IT 329204-97-9P 329205-88-1P 878018-86-1P
878018-92-9P 878018-97-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of methyl[(pyridinyl)ethynyl]thiazole derivs. and study of their activity as noncompetitive metabotropic glutamate receptor subtype-5 (mGluR5) antagonists)
RN 329204-97-9 CAPLUS
CN Pyridine, 3-bromo-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



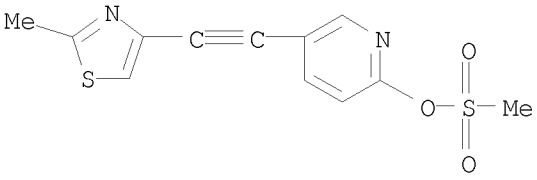
RN 329205-88-1 CAPLUS
CN Pyridine, 2-methoxy-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



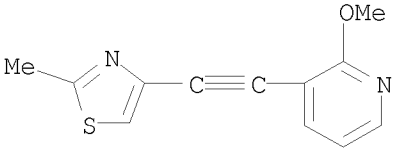
RN 878018-86-1 CAPLUS
CN Pyridine, 3-ethynyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



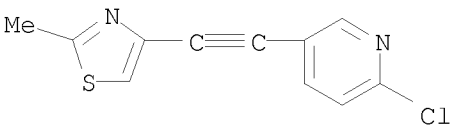
RN 878018-92-9 CAPLUS
CN 2-Pyridinol, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-, 2-methanesulfonate (CA INDEX NAME)



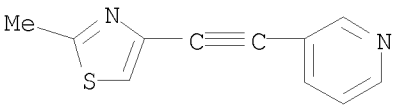
RN 878018-97-4 CAPLUS
CN Pyridine, 2-methoxy-3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



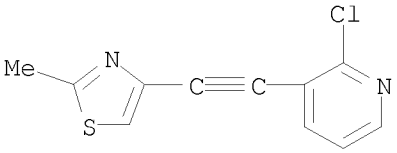
IT 329204-13-9P 329205-68-7P 686768-57-0P
767277-26-9P 878018-47-4P 878018-49-6P
878018-50-9P 878018-54-3P 878018-81-6P
878018-84-9P 878018-89-4P 878018-94-1P
878018-95-2P 878018-96-3P 878019-01-3P
878019-04-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of methyl[(pyridinyl)ethynyl]thiazole derivs. and study of their activity as noncompetitive metabotropic glutamate receptor subtype-5 (mGluR5) antagonists)
RN 329204-13-9 CAPLUS
CN Pyridine, 2-chloro-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



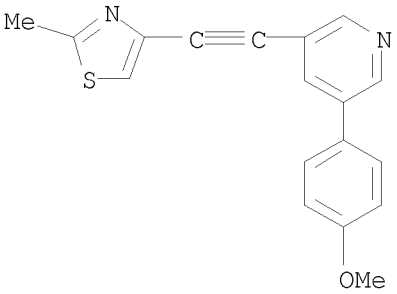
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



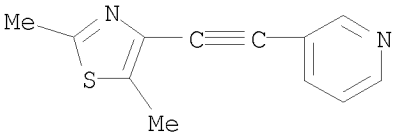
RN 686768-57-0 CAPLUS
CN Pyridine, 2-chloro-3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



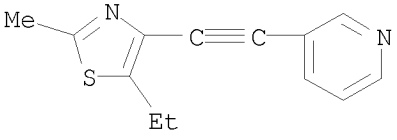
RN 767277-26-9 CAPLUS
CN Pyridine, 3-(4-methoxyphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



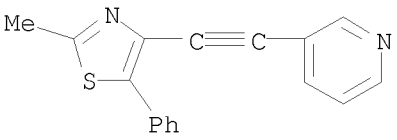
RN 878018-47-4 CAPLUS
CN Pyridine, 3-[2-(2,5-dimethyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



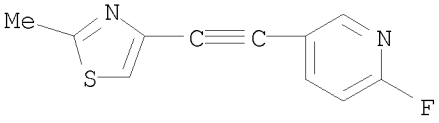
RN 878018-49-6 CAPLUS
CN Pyridine, 3-[2-(5-ethyl-2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



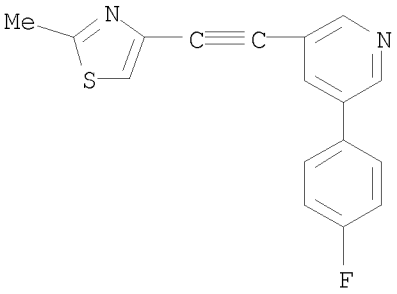
RN 878018-50-9 CAPLUS
CN Pyridine, 3-[2-(2-methyl-5-phenyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



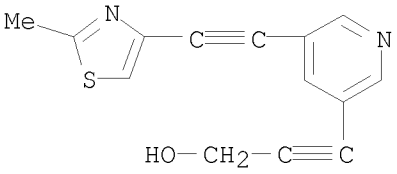
RN 878018-54-3 CAPLUS
CN Pyridine, 2-fluoro-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



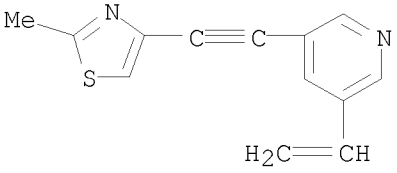
RN 878018-81-6 CAPLUS
CN Pyridine, 3-(4-fluorophenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 878018-84-9 CAPLUS
CN 2-Propyn-1-ol, 3-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-3-pyridinyl]- (CA INDEX NAME)



RN 878018-89-4 CAPLUS
CN Pyridine, 3-ethenyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 878018-94-1 CAPLUS
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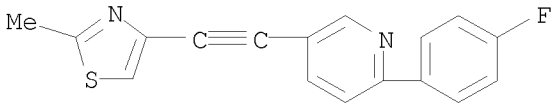
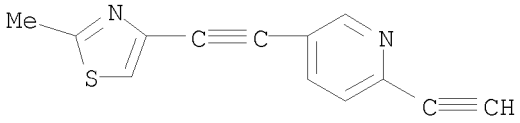
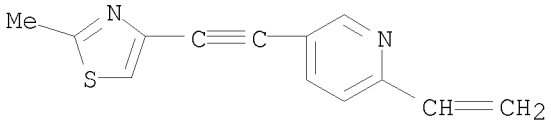


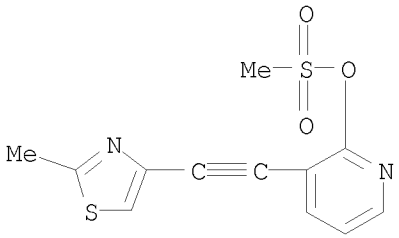
RN 878018-95-2 CAPLUS
CN Pyridine, 2-ethynyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



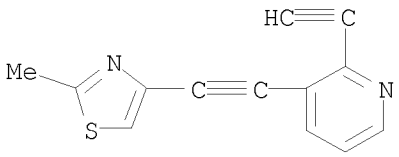
RN 878018-96-3 CAPLUS
CN Pyridine, 2-ethenyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 878019-01-3 CAPLUS
CN 2-Pyridinol, 3-[2-(2-methyl-4-thiazolyl)ethynyl]-, 2-methanesulfonate (CA INDEX NAME)



RN 878019-04-6 CAPLUS
CN Pyridine, 2-ethynyl-3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

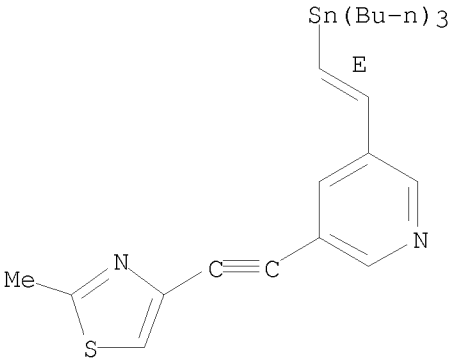


IT 878018-88-3P 878018-91-8P 878018-93-0P
878018-99-6P 878019-02-4P 878019-03-5P

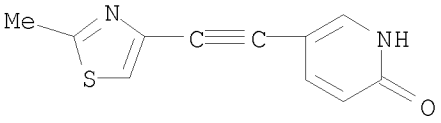
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of methyl[(pyridinyl)ethynyl]thiazole derivs. and study of their activity as noncompetitive metabotropic glutamate receptor subtype-5 (mGluR5) antagonists)

RN 878018-88-3 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]-5-[(1E)-2-(tributylstannyl)ethenyl]- (CA INDEX NAME)

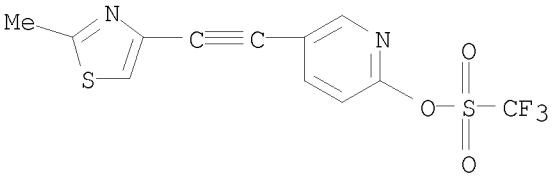
Double bond geometry as shown.



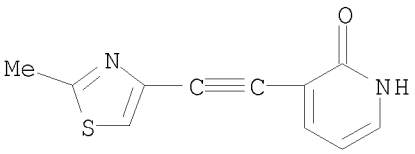
RN 878018-91-8 CAPLUS
CN 2(1H)-Pyridinone, 5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



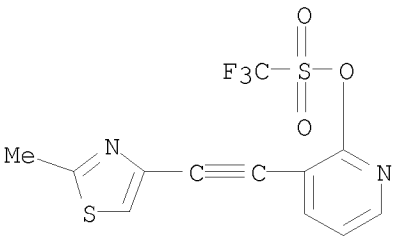
RN 878018-93-0 CAPLUS
CN Methanesulfonic acid, 1,1,1-trifluoro-, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl ester (CA INDEX NAME)



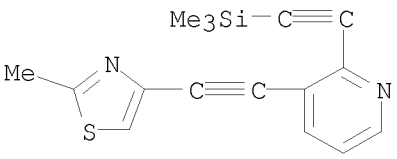
RN 878018-99-6 CAPLUS
CN 2(1H)-Pyridinone, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 878019-02-4 CAPLUS
CN Methanesulfonic acid, 1,1,1-trifluoro-, 3-[2-(2-methyl-4-thiazolyl)ethynyl]-2-pyridinyl ester (CA INDEX NAME)



RN 878019-03-5 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]-2-[2-(trimethylsilyl)ethynyl]- (CA INDEX NAME)



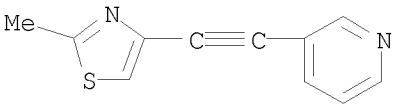
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 38 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1277087 CAPLUS
DOCUMENT NUMBER: 144:120871
TITLE: In vitro metabolic studies on the selective metabotropic glutamate receptor sub-type 5 (mGluR5) antagonist 3-[(2-methyl-1,3-thiazol-4-yl) ethynyl]-pyridine (MTEP)
AUTHOR(S): Green, Mitchell D.; Yang, Xiaoqing; Cramer, Merryl; King, Christopher D.
CORPORATE SOURCE: Medicinal Chemistry, DMPK, Merck Research Laboratories San Diego, San Diego, CA, 92121, USA
SOURCE: Neuroscience Letters (2006), 391(3), 91-95
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Metabotropic glutamate receptors (mGluR) are G-protein-coupled receptors that play a major role in modulatory pathways in the CNS and have been suggested to have pharmacol. implications in pain, psychiatric disorders and other neurol. states. 3-[(2-Methyl-1,3-thiazol-4-yl)ethynyl]pyridine (MTEP) is a specific and selective antagonist for the mGluR sub-type 5. Previous studies using rat liver microsomes showed that the major oxidative metabolites of MTEP are a hydroxymethyl metabolite (M1), two oxides (M2 and M4), a thiazole-ring opened metabolite (M3) and CO2 (M5). In the present study, the authors examined the metabolism of MTEP in liver microsomes and expressed rat and human CYP isoforms. In rat liver microsomes, metabolic stability studies accurately predicted the in vivo clearance for MTEP. Incubation of MTEP with expressed rat and human CYP isoforms showed that CYP1A and CYP2C isoforms are primarily responsible for the metabolism of this compound The results suggest that species

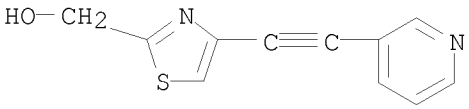
differences in MTEP metabolism is possible and could contribute to specie-differences in biol. effects of the compound

IT 329205-68-7D, MTEP, metabolites 873211-54-2 873211-55-3
RL: BSU (Biological study, unclassified); BIOL (Biological study) (in vitro metabolism of selective metabotropic glutamate receptor sub-type 5 (mGluR5) antagonist MTEP)

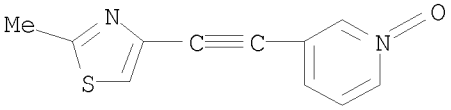
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 873211-54-2 CAPLUS
CN 2-Thiazolemethanol, 4-[2-(3-pyridinyl)ethynyl]- (CA INDEX NAME)

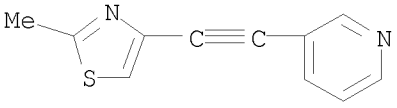


RN 873211-55-3 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]-, 1-oxide (CA INDEX NAME)



IT 329205-68-7, MTEP
RL: PKT (Pharmacokinetics); BIOL (Biological study) (in vitro metabolism of selective metabotropic glutamate receptor sub-type 5 (mGluR5) antagonist MTEP)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

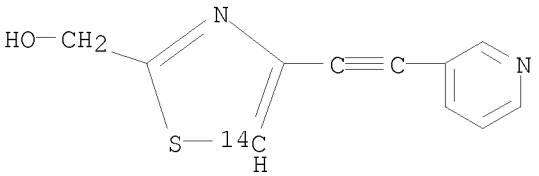
L4 ANSWER 39 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1205641 CAPLUS
DOCUMENT NUMBER: 144:205101
TITLE: In vitro microsomal metabolic studies on a selective mGluR5 antagonist MTEP: Characterization of in vitro metabolites and identification of a novel thiazole

ring opening aldehyde metabolite
AUTHOR(S): Yang, X.; Chen, W.
CORPORATE SOURCE: Drug Metabolism and Pharmacokinetics Group, Department of Medicinal Chemistry, Merck Research Laboratories, San Diego, CA, USA
SOURCE: Xenobiotica (2005), 35(8), 797-809
CODEN: XENOBH; ISSN: 0049-8254
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In vitro liver microsomal studies revealed that [14C] MTEP (3-[(2-methyl-1,3-thiazol-4-yl)ethynyl] pyridine) was metabolized into three major oxidative metabolites. Metabolite 1 (M1) was shown to be a hydroxymethyl metabolite; M2 was shown to be a pyridine oxide. Moreover, a novel aldehyde metabolite (M3) was identified from mouse liver microsomes. The structure of the aldehyde M3 was elucidated by LC/MS/MS. In addition, methoxyamine, an aldehyde-trapping agent, and accurate mass measurement using a high-resolution quadrupole-time of flight (Q-TOF) instrument, were used to confirm the proposed thiazole ring-opening structure of M3. A mechanism for aldehyde M3 formation was postulated based on MTEP incubation studies with 18O2 and H2 18O using mouse liver microsomes. MTEP was initially oxidized at sulfur, followed by subsequent C4-C5 of thiazole epoxidn., thiozole ring opening and further oxidative desulfation. This proposed thiazole ring-opening mechanism might represent a novel metabolism pathway for xenobiotics containing a thiazole moiety.

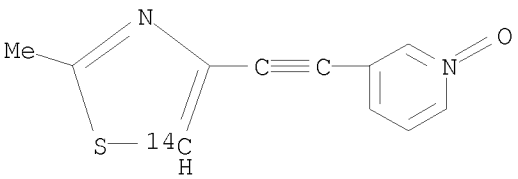
Species differences in the metabolism of MTEP were observed in mouse, rat, dog, monkey and human liver microsomes. Mouse appears to generate all three oxidative metabolites to a greater extent than other species examined

IT 876062-44-1 876062-45-2 876062-47-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro microsomal metabolic studies on mGluR5 antagonist MTEP and its metabolites)

RN 876062-44-1 CAPLUS
CN 2-Thiazole-5-14C-methanol, 4-(3-pyridinylethynyl)- (9CI) (CA INDEX NAME)

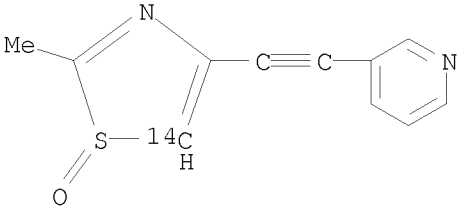


RN 876062-45-2 CAPLUS
CN Pyridine, 3-[(2-methyl-4-thiazolyl-5-14C)ethynyl]-, 1-oxide (9CI) (CA INDEX NAME)

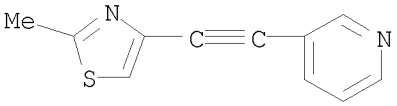


RN 876062-47-4 CAPLUS
CN Pyridine, 3-[(2-methyl-1-oxido-4-thiazolyl-5-14C)ethynyl]- (9CI) (CA

INDEX NAME)



IT 329205-68-7, MTEP
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro microsomal metabolic studies on mGluR5 antagonist MTEP and its metabolites)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



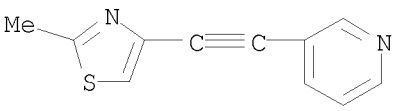
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 40 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1182395 CAPLUS
DOCUMENT NUMBER: 144:65371
TITLE: The metabotropic glutamate 5 receptor antagonist 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]-pyridine reduces ethanol self-administration in multiple strains of alcohol-preferring rats and regulates olfactory glutamatergic systems
AUTHOR(S): Cowen, Michael S.; Djouma, Elvan; Lawrence, Andrew J.
CORPORATE SOURCE: Howard Florey Institute, University of Melbourne, Victoria, Australia
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2005), 315(2), 590-600
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The metabotropic glutamate 5 receptor (mGlu5) receptor has been implicated as having a role in pain modulation, anxiety, and depression, as well as drug-seeking behavior. In the present study, we examined the effect of the selective mGlu5 receptor antagonist 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]-pyridine (MTEP) on operant ethanol self-administration by two strains of rats, the Fawn-Hooded (FH) rat and the inbred alc.-preferring (iP) rat. MTEP (2 mg/kg i.p.) caused a significant reduction in responding for ethanol by both strains of rats; however, in the iP rats, MTEP also induced apparent sedation at this dose, although still reduced alc. responding at lower doses. Chronic MTEP (2 mg/kg/day) caused a significant reduction in ethanol consumption by FH rats in a two-bottle preference test; however,

chronic treatment with this dose had no effect on anxiety-like behavior or depressive-like behavior in FH rats, suggesting the dose used was subthreshold for anxiolytic or antidepressive-like effects. Finally, repeated dosing with MTEP (2 mg/kg i.p.) caused significant redns. in expression of the mRNA encoding the NR1 subunit of the N-methyl-D-aspartate receptor and the GluR2 subunit of the α-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor in the cingulate cortex. A significant decrease in NR1 expression also occurred in the piriform cortex. Chronic MTEP also caused a significant decrease in mGlu5 gene expression and a significant increase in dopamine transporter and dopamine D2-like receptor binding within the olfactory tubercle. Collectively, these data suggest that MTEP can reduce alc.-seeking behavior in different rodent models of alcoholism, and this effect is associated with regulation of cortical glutamate systems, particularly those in olfactory-related regions.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabotropic glutamate 5 receptor antagonist MTEP reduces ethanol self-administration in multiple strains of alc.-preferring rats and regulates olfactory glutamatergic systems)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

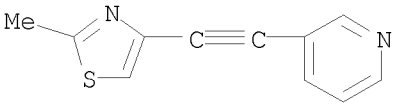
L4 ANSWER 41 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1091076 CAPLUS
DOCUMENT NUMBER: 144:121431
TITLE: Inhibition of transient lower esophageal sphincter relaxation and gastroesophageal reflux by metabotropic glutamate receptor ligands
AUTHOR(S): Frisby, Claudine L.; Mattsson, Jan P.; Jensen, Joergen M.; Lehmann, Anders; Dent, John; Blackshaw, L. Ashley
CORPORATE SOURCE: Nerve-Gut Research Laboratory, Royal Adelaide Hospital, Adelaide, Australia
SOURCE: Gastroenterology (2005), 129(3), 995-1004
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background & Aims: Transient lower esophageal sphincter relaxation (TLESR) is the major mechanism of gastroesophageal acid reflux. TLESR is mediated via vagal pathways, which may be modulated by metabotropic glutamate receptors (mGluRs). Group I mGluRs (mGluR1 and 5) have excitatory effects on neurons, whereas group II (mGluR2 and 3) and group III (mGluR4, 6, 7, and 8) are inhibitory. This study determined the effect of mGluRs on triggering of TLESR and reflux in an established conscious ferret model. Methods: Esophageal manometric/pH studies were performed in ferrets with chronic esophagostomies. TLESR were induced by a gastric load of 25 mL glucose (pH 3.5) and 30 mL air. Results: In control treated animals, gastric load induced 3.52 ± 0.46 TLESRs per 47-min study, 89.7% of

which were associated with reflux episodes (n = 16). The mGluR5 antagonist MPEP inhibited TLESR dose dependently, with maximal 71% ± 7% inhibition at 35 μmol/kg (n = 9; P < .0001). MPEP also significantly reduced reflux episodes (P < .001) and increased basal lower esophageal sphincter pressure (P < .05). MPEP inhibited swallowing dose dependently, suggesting a common action on trigger mechanisms for swallowing and TLESR. The more selective analog, MTEP, had more potent effects (90% ± 6% inhibition TLESR at 40 μmol/kg; n = 8; P < .0001). In contrast, the group I agonist DHPG tended to increase TLESR. The group II agonist (2R, 4R)-APDC was ineffective, whereas the group III agonist L-AP4 slightly reduced TLESR (33% at 11 μmol/kg; P < .05). The selective mGluR5 agonist (S)-3, 4-DCPG inhibited TLESR by 54% at 15 μmol/kg (P < .01). Conclusions: mGluR5 antagonists potently inhibit TLESR and reflux in ferrets, implicating mGluR5 in the mechanism of TLESR. MGluR5 antagonists are therefore promising as therapy for patients with GERD.

IT 329205-68-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabotropic glutamate receptor inhibitor 3-([2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine inhibited TLESR and swallowing, reduced reflux episode and increased basal lower esophageal sphincter pressure in ferret with chronic esophagostomies)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

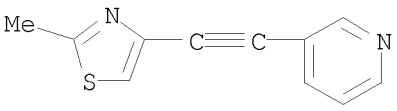
L4 ANSWER 42 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:861882 CAPLUS
DOCUMENT NUMBER: 143:298928
TITLE: Potential antidepressant-like effect of MTEP, a potent and highly selective mGluR5 antagonist
AUTHOR(S): Palucha, Agnieszka; Branski, Piotr; Szewczyk, Bernadeta; Wieronska, Joanna M.; Klak, Kinga; Pilc, Andrzej
CORPORATE SOURCE: Institute of Pharmacology, Polish Academy of Sciences, Krakow, 31-343, Pol.
SOURCE: Pharmacology, Biochemistry and Behavior (2005), 81(4), 901-906
CODEN: PBBHAU; ISSN: 0091-3057
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The involvement of glutamate in the pathophysiol. of depression has been suggested by a number of expts. It was well established that compds., which decreased glutamatergic transmission via blockade of NMDA receptor, produced antidepressant-like action in animal tests and models. The present study was carried out to investigate whether a selective mGluR5 antagonist 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]-pyridine (MTEP) induces antidepressant-like effects after i.p. injections in male Wistar rats or male C57BL/6J mice. Potential antidepressant-like activity of MTEP was evaluated using the forced swimming test (FST) in rats, the tail

suspension test (TST) in mice and the olfactory bulbectomy (OB) model of depression in rats. The results of our studies showed, that MTEP (0.3-3 mg/kg) produced a significant dose-dependent decrease in the immobility time of mice in the TST, however, at doses of 1 or 10 mg/kg, it did not influence the behavior of rats in the FST in rats. Moreover, the repeated administration of MTEP (1 mg/kg) attenuated the OB-related hyperactivity of rats in the open field test, in the manner similar to that seen following chronic (but not acute) treatment with typical antidepressant drugs. These data suggest that MTEP, which is considered to be a potential therapeutic agent, may play a role in the therapy of depression.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potential antidepressant-like effect of MTEP, potent and highly selective mGluR5 antagonist)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 43 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:844852 CAPLUS
DOCUMENT NUMBER: 143:279142
TITLE: MTEP, a new selective antagonist of the metabotropic glutamate receptor subtype 5 (mGluR5), produces antiparkinsonian-like effects in rats
AUTHOR(S): Ossowska, K.; Konieczny, J.; Wolfarth, S.; Pilc, A.
CORPORATE SOURCE: Department of Neuro-Psychopharmacology, Institute of Pharmacology, Polish Academy of Sciences, Krakow, 31-343, Pol.
SOURCE: Neuropharmacology (2005), 49(4), 447-455
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

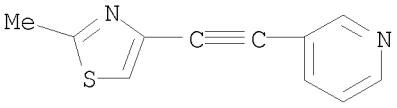
AB The aim of the present study was to examine a potential antiparkinsonian-like action of 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (MTEP), a new non-competitive antagonist of mGluR5, in the rat models. This compound has affinity for mGluR5 in a nanomolar concentration range and seems to be superior to the earlier known antagonists in terms of its specificity and bioavailability. Catalepsy and muscle rigidity induced by haloperidol administered at doses of 0.5 and 1 mg/kg were regarded as models of parkinsonian akinesia and muscle rigidity, resp. MTEP at doses between 0.5 and 3 mg/kg i.p. decreased the haloperidol-induced muscle rigidity measured as an increased muscle resistance of the rat's hind leg in response to passive extension and flexion at the ankle joint. The strongest and the longest effect was observed after the dose of 1 mg/kg. MTEP (0.5-3 mg/kg i.p.) also reduced the haloperidol-induced increase in electromyog. (EMG) activity recorded in the gastrocnemius and tibialis anterior muscles. MTEP (3 and 5 mg/kg i.p.) inhibited the catalepsy induced by haloperidol. The present study

confirms earlier suggestions that the antagonists of mGluR5 may possess antiparkinsonian properties. However, selective mGluR5 antagonists may be more effective in inhibiting parkinsonian muscle rigidity than parkinsonian akinesia.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mGluR5 antagonist MTEP produces antiparkinsonian-like effects in rats)

RN 329205-68-7 CAPLUS

CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 44 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:580046 CAPLUS

DOCUMENT NUMBER: 143:260117

TITLE: mGluR5, but not mGluR1, antagonist modifies MK-801-induced locomotor activity and deficit of prepulse inhibition

AUTHOR(S): Pietraszek, M.; Gravius, A.; Schaefer, D.; Weil, T.; Trifanova, D.; Danysz, W.

CORPORATE SOURCE: Preclinical R&D, Merz Pharmaceuticals, Frankfurt am Main, 60318, Germany

SOURCE: Neuropharmacology (2005), 49(1), 73-85
CODEN: NEPHBW; ISSN: 0028-3908

PUBLISHER: Elsevier B.V.

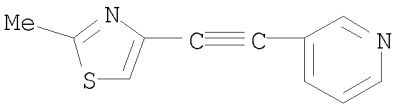
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hypoglutamatergic theory of schizophrenia is substantiated by observation that high affinity uncompetitive antagonists of NMDA receptors such as PCP can induce psychotic symptoms in humans. Recently, metabotropic glutamate receptors of the mGluR5 type have also been discussed as possible players in this disease. However, less is known about the potential contribution of mGluR1 in schizophrenia. Therefore, the aim of the present study was to compare the effect of selective mGluR1 antagonist EMQMCM, (3-ethyl-2-methyl-quinolin-6-yl)-(4-methoxy-cyclohexyl)-methanone methanesulfonate and mGluR5 antagonist MTEP ([(2-methyl-1,3-thiazol-4-yl) ethynyl] pyridine) either alone or in combination with (+)MK-801 in a prepulse inhibition (PPI) model and locomotor activity tests. Addnl., the effect of both mGluR1 and mGluR5 antagonists on (+)MK-801-evoked ataxia was tested. In contrast to (+)MK-801, which induced disruption of PPI, neither MTEP (1.25-5 mg/kg) nor EMQMCM (0.5-4 mg/kg) altered the PPI. However, MTEP, but not EMQMCM, enhanced disruption of PPI induced by (+)MK-801. Although neither mGluR1 nor mGluR5 antagonists given alone changed locomotor activity of rats, MTEP at 5 mg/kg potentiated the effect of (+)MK-801 while EMQMCM (up to 4 mg/kg) turned out to be ineffective. On the other hand, EMQMCM, but not MTEP, enhanced ataxia evoked by MK-801. The present results demonstrate that blockade of mGluR1 and mGluR5 evokes different effects on behavior induced by NMDA receptor antagonists.

IT 329205-68-7, MTEP
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mGluR5, but not mGluR1, antagonist modifies MK-801-induced locomotor activity and deficit of prepulse inhibition)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



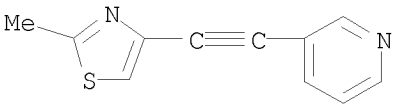
REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 45 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:511877 CAPLUS
DOCUMENT NUMBER: 143:126567
TITLE: Neuroprotective activity of the mGluR5 antagonists MPEP and MTEP against acute excitotoxicity differs and does not reflect actions at mGluR5 receptors
AUTHOR(S): Lea, Paul M.; Movsesyan, Vilen A.; Faden, Alan I.
CORPORATE SOURCE: Department of Neuroscience, Georgetown University Medical Center, Washington, DC, USA
SOURCE: British Journal of Pharmacology (2005), 145(4), 527-534
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Neuroprotection has been reported after either activation or blockade of the group I metabotropic glutamate receptor subtype 5 (mGluR5). However, some recent evidence suggests that protection provided by mGluR5 antagonists may reflect their ability to inhibit N-methyl-D-aspartate (NMDA) receptor activity. Here, in both rat and mouse cortical neurons, we compare the neuroprotective actions of two mGluR5 antagonists: 2-methyl-6-(phenylethynyl)-pyridine (MPEP), which has been commonly used and 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (MTEP), a more recently developed compound believed to have greater mGluR5 selectivity. We have previously shown that MPEP directly reduces single-channel NMDA receptor open time at the same concns. (20 μM or greater) that show neuroprotection, whereas MPEP antagonizes mGluR5 agonist ((RS)-2-chloro-5-hydroxyphenylglycine (CHPG))-induced changes in inositol phosphates (IP) at concns. as low as 0.2 μM. In the present studies, MTEP significantly inhibited CHPG-mediated IP hydrolysis at concns. as low as 0.02 μM. In contrast to MPEP, which significantly reduced glutamate- or NMDA-mediated cell death in primary rat neuronal cultures at a concentration of 20 μM, small neuroprotective effects were observed with MTEP
only at a concentration of 200 μM. Neither MPEP- nor MTEP-mediated mGluR5 inhibition had any effect on etoposide-induced apoptotic cell death. In rat cortical neurons, the neuroprotective effects of MTEP at very high concns., like those of MPEP, reflect ability to directly reduce NMDA receptor peak and steady-state currents. We also compared the effects of MPEP and MTEP in primary cortical neuronal cultures from parental and mGluR5 knockout mice. Both agents were neuroprotective, at high concns. in normal as well as in the knockout cultures. In contrast to rat cortical neurons, neither MPEP nor MTEP appears to directly alter NMDA receptor activity. Combined, these studies support the conclusion that MTEP has greater mGluR5 selectivity than MPEP, and that neuroprotection

provided by either antagonist in neuronal cultures does not reflect inhibition of mGluR5 receptors.

IT 329205-68-7, MTEP
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotective activity of mGluR5 antagonists MPEP and MTEP against acute excitotoxicity differs and does involve mGluR5 receptors)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



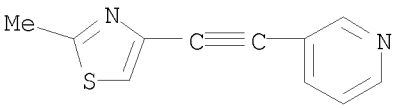
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 46 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:412797 CAPLUS
DOCUMENT NUMBER: 143:19835
TITLE: Selective mGlu5 receptor antagonist MTEP attenuates naloxone-induced morphine withdrawal symptoms
AUTHOR(S): Palucha, Agnieszka; Branski, Piotr; Pilc, Andrzej
CORPORATE SOURCE: Institute of Pharmacology, Polish Academy of Sciences, Krakow, PL 31-343, Pol.
SOURCE: Polish Journal of Pharmacology (2004), 56(6), 863-866
CODEN: PJPAE3; ISSN: 1230-6002
PUBLISHER: Polish Academy of Sciences, Institute of Pharmacology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several lines of evidence suggest a crucial involvement of glutamate in the mechanism of drug addiction. The involvement of group I mGlu receptors in the mechanism of addiction has also been proposed. Given the recent discovery of selective and brain penetrable mGlu5 receptor antagonists, the effects of 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]-pyridine (MTEP) were evaluated in the naloxone-precipitated morphine withdrawal model. Expts. were performed on male C57BL/6J (20-25 g) mice. Mice were rendered morphine-dependent and withdrawal was precipitated with naloxone. Two hours and 15 min after the last dose of morphine, mice were injected with a mGlu5 receptor antagonist. MTEP (1-10 mg/kg) in a dose-dependent manner inhibited the naloxone-induced symptoms of morphine withdrawal in morphine-dependent mice, remaining without any effect on the locomotor activity of mice. The data suggest that selective mGlu5 receptor antagonists may play a role in the therapy of drug-dependence states.

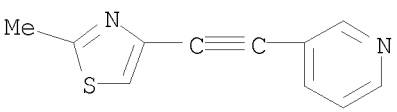
IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective mGlu5 receptor antagonist 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]-pyridine dose-dependently attenuated naloxone-induced symptoms of morphine withdrawal symptoms without locomotor activity in morphine-dependent mouse model)

RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 47 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:387247 CAPLUS
DOCUMENT NUMBER: 143:1087
TITLE: Anxiolytic-like effects of mGlu1 and mGlu5 receptor antagonists in rats
AUTHOR(S): Pietraszek, Malgorzata; Sukhanov, Ilia; Maciejak, Piotr; Szyndler, Janusz; Gravius, Andreas; Wislowska, Aleksandra; Plaznik, Adam; Bespalov, Anton Y.; Danysz, Wojciech
CORPORATE SOURCE: Preclinical R&D, Merz Pharmaceuticals GmbH, Frankfurt am Main, 60318, Germany
SOURCE: European Journal of Pharmacology (2005), 514(1), 25-34
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of the present study was to compare anxiolytic activity of the metabotropic glutamate receptor 1 (mGlu) antagonist, EMQMCM ((3-ethyl-2-methyl-quinolin-6-yl)-(4-methoxy-cyclohexyl)-methanone methanesulfonate) and the mGlu5 receptor antagonist MTEP ([(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine) and MPEP (2-methyl-6-(phenylethynyl)pyridine) in animal models of anxiety. In the elevated plus maze, diazepam (1 mg/kg), but not the mGlu1 or mGlu5 receptor antagonists induced anxiolytic-like effects. Meanwhile, MTEP (2.5 and 5 mg/kg), EMQMCM (5 mg/kg), and diazepam (2 mg/kg) all significantly inhibited fear potentiated startle. In the contextual fear conditioning test, MTEP (1.25 and 2.5 but not 5 mg/kg) and EMQMCM (0.6 to 5 mg/kg) attenuated freezing responding. In the Geller-Seifter conflict test, MPEP (1 and 3 mg/kg), MTEP (3 mg/kg), chlordiazepoxide (10 and 20 mg/kg) and midazolam (1 mg/kg) all facilitated punished responding, while ECMQCM failed to produce any significant effects up to 3 mg/kg dose. To summarize, the present data further support a significant anxiolytic potential of group I mGlu receptor antagonists, while suggesting the effects of mGlu1 receptor antagonists may depend on the exptl. procedure and may be qual. different from those of mGlu5 receptor antagonists.
IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anxiolytic-like effects of mGlu1 and mGlu5 receptor antagonists in rats)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

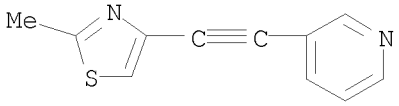


REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 48 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:330449 CAPLUS
DOCUMENT NUMBER: 142:368062
TITLE: Metabotropic glutamate receptor mGlu5 is a mediator of appetite and energy balance in rats and mice
AUTHOR(S): Bradbury, Margaret J.; Campbell, Una; Giracello, Darlene; Chapman, Deborah; King, Chris; Tehrani, Lida; Cosford, Nicholas D. P.; Anderson, Jeff; Varney, Mark A.; Strack, Alison M.
CORPORATE SOURCE: Department of Neuropharmacology, Merck Research Laboratories, San Diego, CA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2005), 313(1), 395-402
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

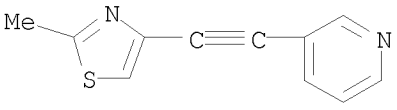
AB The metabotropic glutamate receptor subtype mGlu5 modulates central reward pathways. Many transmitter systems within reward pathways affect feeding. We examined the potential role of mGlu5 in body weight regulation using genetic and pharmacol. approaches. Adult mice lacking mGlu5, mGluR5-/-, weighed significantly less than littermate controls (mGluR5+/+), despite no difference in ad libitum food intake. After overnight food deprivation, mGluR5-/- mice ate significantly less than their mGluR5+/+ controls when refeeding. When on a high fat diet, mGluR5-/- mice weighed less and had decreased plasma insulin and leptin concns. The selective mGlu5 antagonist MTEP [3-[(2-methyl-1,3-thiazol-4-yl)-ethynyl]-pyridine; 15 mg/kg s.c.] reduced refeeding after overnight food deprivation in mGluR5+/+, but not mGluR5-/- mice, demonstrating that feeding suppression is mediated via a mGlu5 mechanism. MTEP (1-10 mg/kg) decreased night-time food intake in rats in a dose-related manner. At 10 mg/kg, MTEP injected at 8.5, 4.5, or 0.5 h before refeeding reduced overnight food intake by approx. .apprx.30%. Diet-induced obese (DIO) and age-matched lean rats were treated for 12 days with MTEP (3 or 10 mg/kg/day s.c.), dexfenfluramine (3 mg/kg/day s.c.), or vehicle. Daily and cumulative food intakes were reduced in DIO rats by MTEP and dexfenfluramine. Weight gain was prevented with MTEP (3 mg/kg), and weight and adiposity loss was seen with MTEP (10 mg/kg) and dexfenfluramine. Caloric efficiency was decreased, suggesting increased energy expenditure. In lean rats, similar, although smaller, effects were observed In conclusion, using genetic and pharmacol. approaches, we have shown that mGlu5 modulates food intake and energy balance in rodents.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); BIOL (Biological study)
(metabotropic glutamate receptor mGlu5 as mediator of appetite and energy balance in rats and mice)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

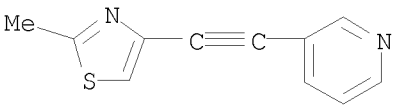
L4 ANSWER 49 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:309176 CAPLUS
DOCUMENT NUMBER: 142:456886
TITLE: Blockade of the mGlu5 receptor decreases basal and stress-induced cortical norepinephrine in rodents
AUTHOR(S): Page, Michelle E.; Szeliga, Paul; Gasparini, Fabrizio; Cryan, John F.
CORPORATE SOURCE: Department of Neurobiology and Anatomy, Drexel University College of Medicine, Philadelphia, PA, 19129, USA
SOURCE: Psychopharmacology (Berlin, Germany) (2005), 179(1), 240-246
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Glutamate, the major excitatory neurotransmitter in the brain mediates its effects by both ionotropic and metabotropic receptor subtypes. Recently, the search for selective ligands for glutamate receptor subtypes has led to the discovery of 2-methyl-6-(phenylethynyl)pyridine (MPEP), an antagonist specific for metabotropic glutamate receptor 5 (mGlu5). This receptor is highly expressed in limbic forebrain regions and is thought to modulate anxiety-related processes. The noradrenergic nucleus locus coeruleus (LC) is an important mediator of stress responses and dysfunction of this system is implicated in affective disorders such as anxiety and depression. The authors sought to assess the effects of mGlu5 receptor antagonists, MPEP and 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (MTEP) on cortical norepinephrine (NE) levels. In vivo microdialysis and high-pressure liquid chromatog. with electrochem. detection (HPLC-ED) were used to assess the effects of mGlu5 antagonism on extracellular NE in the frontal cortex, a major terminal field of the LC. Blockade of the mGlu5 receptor elicited significant redns. in extracellular NE in the frontal cortex. The benzodiazepine diazepam also reduced cortical NE. Furthermore, MPEP administration attenuated stress-induced increases in extracellular NE. Taken together, these data show that MPEP and MTEP, through their blockade of the mGlu5, reduce extracellular norepinephrine, the impact of which may contribute to their anxiolytic actions.
IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blockade of mGlu5 receptor decreases basal and stress-induced cortical norepinephrine in rodents)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

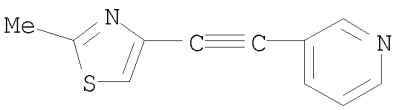
L4 ANSWER 50 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:309170 CAPLUS
DOCUMENT NUMBER: 142:456881
TITLE: The antinociceptive and anxiolytic-like effects of the metabotropic glutamate receptor 5 (mGluR5) antagonists, MPEP and MTEP, and the mGluR1 antagonist, LY456236, in rodents: a comparison of efficacy and side-effect profiles
AUTHOR(S): Varty, Geoffrey B.; Grilli, Mariagrazia; Forlani, Angelo; Fredduzzi, Silva; Grzelak, Michael E.; Guthrie, Donald H.; Hodgson, Robert A.; Lu, Sherry X.; Nicolussi, Elisa; Pond, Annamarie J.; Parker, Eric M.; Hunter, John C.; Higgins, Guy A.; Reggiani, Angelo; Bertorelli, Rosalia
CORPORATE SOURCE: Department of Neurobiology, Schering Plough Research Institute, Kenilworth, NJ, 07033, USA
SOURCE: Psychopharmacology (Berlin, Germany) (2005), 179(1), 207-217
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Modulation of metabotropic glutamate receptor (mGluR) subtypes represents a novel approach for the treatment of neurol. and psychiatric disorders. This study was conducted to investigate the role of the mGluR5 and mGluR1 subtypes in the modulation of pain and anxiety. The mGluR5 antagonists, 2-methyl-6-(phenylethynyl)pyridine (MPEP) and 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (MTEP), and the mGluR1 antagonist, (4-methoxy-phenyl)-(6-methoxy-quinazolin-4-yl)-amine HCl (LY456236), were tested in models of pain [mouse formalin test, rat spinal nerve ligation (SNL)] and anxiety [Vogel conflict, conditioned lick suppression (CLS)], and their efficacious effects were compared to any associated side effects. The systemic administration of MPEP, MTEP, and LY456236 reduced hyperalgesia induced by formalin and mech. allodynia following SNL. However, only LY456236 completely reversed the allodynia. In the anxiety models, MPEP (3-30 mg/kg), MTEP (3-10 mg/kg), and LY456236 (10-30 mg/kg) produced anxiolytic-like effects similar to the benzodiazepine, chlordiazepoxide (CDP, 6 mg/kg). However, only MPEP and MTEP were able to produce a level of anxiolysis comparable to CDP. In a series of tests examining potential side effects, MPEP and MTEP reduced body temperature and locomotor activity and impaired operant responding for food and rotarod performance at doses of 3-30 and 1-30 mg/kg, resp. LY456236 reduced operant responding at 30 mg/kg. Both mGluR5 and mGluR1 antagonists are effective in models of pain and anxiety. However, an mGluR1 antagonist was more efficacious than the 2 mGluR5 antagonists in the pain models, which, conversely, appeared more efficacious in the anxiety models. These findings support the potential utility of mGluR5 and mGluR1 antagonists for both the treatment of chronic pain and as novel anxiolytics.
IT 329205-68-7, MTEP
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antinociceptive and anxiolytic-like effects of mGluR5 and mGluR1 antagonist, in rodents)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 51 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:227480 CAPLUS
DOCUMENT NUMBER: 143:19795
TITLE: Effects of mGlu1 and mGlu5 receptor antagonists on negatively reinforced learning
AUTHOR(S): Gravius, A.; Pietraszek, M.; Schaefer, D.; Schmidt, W. J.; Danysz, W.
CORPORATE SOURCE: Preclinical R & D, Merz Pharmaceuticals, Frankfurt am Main, Germany
SOURCE: Behavioural Pharmacology (2005), 16(2), 113-121
CODEN: BPHAEL; ISSN: 0955-8810
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Effects on aversive learning of the novel highly selective mGlu5 receptor antagonist [(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (MTEP) and mGlu1 receptor antagonist (3-ethyl-2-methyl-quinolin-6-yl)-(4-methoxy-cyclohexyl)-methanone methanesulfonate (EMQMCM) were tested, after systemic administration, in the passive avoidance (PA) and fear potentiated startle (FPS) paradigms. Both MTEP at 10 mg/kg and EMQMCM at 5 and 10 mg/kg, given 30 min before training, impaired acquisition of the passive avoidance response (PAR). Co-administration of MTEP and EMQMCM at doses ineffective when administered alone, produced anterograde amnesia when given 30 min before the acquisition phase. Neither EMQMCM (5 mg/kg) nor MTEP (10 mg/kg) impaired retention of the PAR after direct post-training injections. EMQMCM (5 mg/kg), but not MTEP (10 mg/kg) blocked the PAR when given 30 min before testing. Pre-training administration of MTEP at doses of 2.5 and 5 mg/kg inhibited fear conditioning in the FPS when tested 24 h later. In contrast, EMQMCM was ineffective. Our findings suggest diverse involvement of mGlu1 and mGlu5 receptors in neg. reinforced learning.
IT 329205-68-7, MTEP
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MTEP with EMQMCM produced dose-dependent amnesia, had no effect on consolidation, EMQMCM but not MTEP impair memory when given before retention suggesting its diverse involvement in neg. reinforced learning in rat)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 52 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:216809 CAPLUS
DOCUMENT NUMBER: 142:298004
TITLE: Preparation of bipyridyl amines and ethers as modulators of metabotropic glutamate receptor-5
INVENTOR(S): Kamenecka, Theodore M.; Vernier, Jean-Michel; Bonnefous, Celine; Govek, Steven P.; Hutchinson, John H.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005021529	A1	20050310	WO 2004-US27916	20040827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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CA 2537141	A1	20050310	CA 2004-2537141	20040827
EP 1664018	A1	20060607	EP 2004-782403	20040827
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CN 1845915	A	20061011	CN 2004-80025067	20040827
JP 2007504229	T	20070301	JP 2006-525369	20040827
IN 2006DN00876	A	20070810	IN 2006-DN876	20060220
US 20070027321	A1	20070201	US 2006-570068	20060301
PRIORITY APPLN. INFO.:			US 2003-499627P P	20030902
			WO 2004-US27916 W	20040827

OTHER SOURCE(S): CASREACT 142:298004; MARPAT 142:298004
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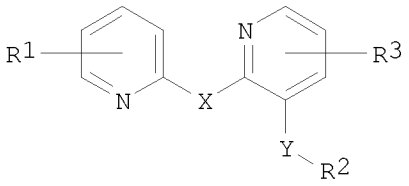
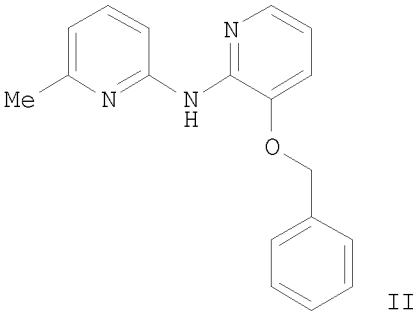


I



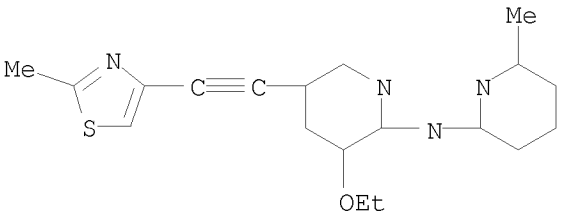
II

AB Title compds. I [R1 = H, (un)substituted-alkyl, -aryl, -cycloalkyl, etc.; R2 = H, (un)substituted-alkyl, -alkenyl, -cycloalkyl, etc.; R3 = H, (un)substituted-aryl, -aryloxy, -heteroaryl, -cycloalkyl, etc.; X = O, S, (un)substituted amine] and their pharmaceutically acceptable salts, are prepared and disclosed as modulators of glutamate receptor-5. Thus, e.g., II, was prepared by microwave assisted Buchwald amination of 3-(benzyloxy)-2-bromopyridine with 6-methylpyridin-2-amine. Calcium Flux or Phosphatidylinositol Hydrolysis (PI) assays were utilized to evaluate the activity of I against glutamate receptor-5 and showed IC50 values of less than 10 μM in the calcium flux assay or inhibition at a concentration of 100 μM in the PI assay. I as modulators of metabotropic glutamate receptor-5 should prove useful in the treatment of mental disorders (e.g., but not limited to, anxiety, depression, dementia), pain, epilepsy, drug dependence, sleep disorders, and obesity.

IT 847902-34-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bipyridyl amines and ethers as modulators of metabotropic glutamate receptor-5)

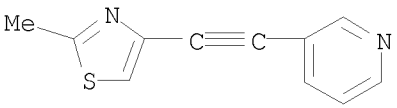
RN 847902-34-5 CAPLUS

CN 2-Pyridinamine, 3-ethoxy-N-(6-methyl-2-pyridinyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 53 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:117701 CAPLUS
DOCUMENT NUMBER: 142:348844
TITLE: The mGlu5 receptor antagonists MPEP and MTEP attenuate behavioral signs of morphine withdrawal and morphine-withdrawal-induced activation of locus coeruleus neurons in rats
AUTHOR(S): Rasmussen, Kurt; Martin, Heidi; Berger, James E.; Seager, Matthew A.
CORPORATE SOURCE: Lilly Research Laboratories, Lilly Corporate Center, Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Neuropharmacology (2005), 48(2), 173-180
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB N-Methyl--aspartate (NMDA) antagonists have been demonstrated to suppress the signs of opiate withdrawal; however, side effects limit their clin. use. Since the metabotropic glutamate (mGlu) 5 receptor has been shown to affect glutamate release and modulate NMDA receptor function, we examined the effects of two selective mGlu5 receptor antagonists, 2-methyl-6-(phenyl-ethynyl)-pyridine (MPEP) and 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (MTEP), on morphine withdrawal. Pretreatment with MPEP or MTEP (1, 3, and 10 mg/kg, i.p.) significantly attenuated behavioral signs of morphine withdrawal. Specifically, both MPEP and MTEP attenuated the occurrence/severity of chews, digging, salivation, and weight loss, and increased the occurrence of erections. Neither compound changed the occurrence of wet-dog shakes, ptosis, irritability, or lacrimation. Both MPEP and MTEP produced a modest, but significant, attenuation of morphine-withdrawal-induced activation of locus coeruleus neurons in anesthetized rats. These results indicate a role for mGlu5 receptors in morphine withdrawal and suggest the potential for mGlu5 antagonists in the treatment of withdrawal from opiates and other drugs of abuse.
IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mGlu5 receptor antagonists MPEP and MTEP attenuate behavioral signs of morphine withdrawal and morphine-withdrawal-induced activation of locus coeruleus neurons in rats)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



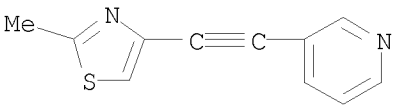
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 54 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:1053982 CAPLUS
DOCUMENT NUMBER: 142:69077
TITLE: Assessing the role of metabotropic glutamate receptor 5 in multiple nociceptive modalities
AUTHOR(S): Zhu, Chang Z.; Wilson, Sonya G.; Mikusa, Joseph P.; Wismer, Carol T.; Gauvin, Donna M.; Lynch, James J.; Wade, Carrie L.; Decker, Michael W.; Honore, Prisca
CORPORATE SOURCE: Neuroscience Research, Global Pharmaceutical Research and Development, Dept. 4N5, Bldg. AP9A, Abbott Laboratories, Abbott Park, IL, 60064-3500, USA
SOURCE: European Journal of Pharmacology (2004), 506(2), 107-118
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Preclin. data, performed in a limited number of pain models, suggest that functional blockade of metabotropic glutamate (mGlu) receptors may be beneficial for pain management. In the present study, effects of 2-methyl-6-(phenylethynyl)-pyridine (MPEP), a potent, selective mGlu5 receptor antagonist, were examined in a wide variety of rodent nociceptive and hypersensitivity models to fully characterize the potential analgesic profile of mGlu5 receptor blockade. Effects of 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (MTEP), as potent and selective as MPEP at mGlu5/mGlu1 receptors but more selective than MPEP at N-methyl-aspartate (NMDA) receptors, were also evaluated in selected nociceptive and side effect models. MPEP (3-30 mg/kg, i.p.) produced a dose-dependent reversal of thermal and mech. hyperalgesia following complete Freund's adjuvant (CFA)-induced inflammatory hypersensitivity. Addnl., MPEP (3-30 mg/kg, i.p.) decreased thermal hyperalgesia observed in carrageenan-induced inflammatory hypersensitivity without affecting paw edema, abolished acetic acid-induced writhing activity in mice, and was shown to reduce mech. allodynia and thermal hyperalgesia observed in a model of post-operative hypersensitivity and formalin-induced spontaneous pain. Furthermore, at 30 mg/kg, i.p., MPEP significantly attenuated mech. allodynia observed in three neuropathic pain models, i.e. spinal nerve ligation, sciatic nerve constriction and vincristine-induced neuropathic pain. MTEP (3-30 mg/kg, i.p.) also potently reduced CFA-induced thermal hyperalgesia. However, at 100 mg/kg, i.p., MPEP and MTEP produced central nerve system (CNS) side effects as measured by rotarod performance and exploratory locomotor activity. These results suggest a role for mGlu5 receptors in multiple nociceptive modalities, though CNS side effects may be a limiting factor in developing mGlu5 receptor analgesic compds.

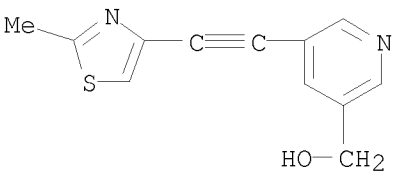
IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(assessing the role of metabotropic glutamate receptor 5 in multiple nociceptive modalities)
RN 329205-68-7 CAPLUS

CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 55 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:1043368 CAPLUS
DOCUMENT NUMBER: 142:106558
TITLE: Synthesis and receptor assay of aromatic-ethynyl-aromatic derivatives with potent mGluR5 antagonist activity
AUTHOR(S): Alagille, David; Baldwin, Ronald M.; Roth, Bryan L.; Wroblewski, Jarda T.; Grajkowska, Ewa; Tamagnan, Gilles D.
CORPORATE SOURCE: Department of Psychiatry, Yale University and VA Connecticut, West Haven, CT, 06516, USA
SOURCE: Bioorganic & Medicinal Chemistry (2004), Volume Date 2005, 13(1), 197-209
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:106558
AB Noncompetitive antagonists of the human metabotropic glutamate receptor subtype 5 (mGluR5) have been implicated as potential therapeutics for the treatment of a variety of nervous system disorders, including pain, anxiety, and drug addiction. To discover novel noncompetitive antagonists to the mGluR5, the authors initiated an SAR study around the known lead compds. MPEP and M-MPEP. Our results pointed out the critical role of the para position of the two aromatic rings, which leads to inactive products and permitted the discovery of potent mGluR5 antagonists (e.g., 16, 25, 28, 34 IC50 = 13.5, 11.9, 21, 15 nM, resp.).
IT 823199-04-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and receptor assay of aromatic-ethynyl-aromatic derivs. with potent mGluR5 antagonist activity)
RN 823199-04-8 CAPLUS
CN 3-Pyridinemethanol, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:1) (CA INDEX NAME)



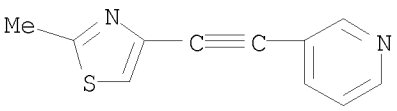
● HCl

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 56 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:870789 CAPLUS
DOCUMENT NUMBER: 142:212131
TITLE: The Behavioral Profile of the Potent and Selective mGlu5 Receptor Antagonist 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (MTEP) in Rodent Models of Anxiety
AUTHOR(S): Busse, Chris S.; Brodkin, Jesse; Tattersall, David; Anderson, Jeffery J.; Warren, Noelle; Tehrani, Lida; Bristow, Linda J.; Varney, Mark A.; Cosford, Nicholas D. P.
CORPORATE SOURCE: Merck Research Laboratories, San Diego, CA, USA
SOURCE: Neuropsychopharmacology (2004), 29(11), 1971-1979
CODEN: NEROEW; ISSN: 0893-133X
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

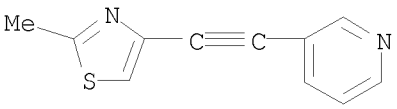
AB Previous reports have demonstrated the anxiolytic effect of the potent and systemically active metabotropic glutamate subtype 5 (mGlu5) receptor antagonist 2-methyl-6-(phenylethynyl)pyridine (MPEP) in rodents. Here, we present evidence for the anxiolytic activity of a novel mGlu5 receptor antagonist, 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (MTEP), in rats and compare its profile to the benzodiazepine receptor agonist diazepam. MTEP occupied mGlu5 receptors in a dose-dependent manner with essentially full receptor occupancy at the highest dose tested (10 mg/kg, i.p.). At doses appropriate for mGlu5 receptor-mediated effects, MTEP significantly reduced fear-potentiated startle and increased punished responding in a modified Geller-Seifter conflict model consistent with an anxiolytic-like profile. In both models, the magnitude of the anxiolytic-like response was similar to that seen with diazepam. In contrast, MTEP decreased unpunished responding to a lesser extent than diazepam and had no effect on rotarod performance when administered either alone or in combination with ethanol. Repeated dosing with MTEP in this model eliminated the increase in punished responding observed with acute dosing. The present results suggest that mGlu5 receptor antagonists lack the side effects seen with benzodiazepines, such as sedation and ethanol interaction, and provide insight into a possible role for mGlu5 receptor antagonists in the modulation of mood disorders.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mGlu5 receptor antagonist MTEP showed anxiolytic effect similar to diazepam and also displayed efficacy in anxiety with no interaction with ethanol, reduced propensity to induce motor impairment in rat model of anxiety)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 57 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:654838 CAPLUS
DOCUMENT NUMBER: 141:325154
TITLE: Discovery of Novel Heteroarylazoles That Are Metabotropic Glutamate Subtype 5 Receptor Antagonists with Anxiolytic Activity
AUTHOR(S): Roppe, Jeffrey; Smith, Nicholas D.; Huang, Dehua; Tehrani, Lida; Wang, Bowei; Anderson, Jeffrey; Brodkin, Jesse; Chung, Janice; Jiang, Xiaohui; King, Christopher; Munoz, Benito; Varney, Mark A.; Prasit, Petpiboon; Cosford, Nicholas D. P.
CORPORATE SOURCE: Merck Research Laboratories, San Diego, CA, 92121, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(19), 4645-4648
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:325154
AB The highly potent, selective, and brain-penetrant metabotropic glutamate subtype 5 (mGlu5) receptor antagonists 3-(5-pyridin-2-yl-2H-tetrazol-2-yl)benzonitrile and 3-fluoro-5-(5-pyridin-2-yl-2H-tetrazol-2-yl)benzonitrile are reported. Compound 3-(5-pyridin-2-yl-2H-tetrazol-2-yl)benzonitrile is active in the rat fear-potentiated startle (FPS) model of anxiety with ED50 = 5.4 mg/kg (po) when dosed acutely. In this model the anxiolytic effects of 3-(5-pyridin-2-yl-2H-tetrazol-2-yl)benzonitrile rapidly tolerate on repeated dosing.
IT 329205-68-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discovery of novel heteroarylazoles that are metabotropic glutamate subtype 5 receptor antagonists with anxiolytic activity)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 58 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:648386 CAPLUS
DOCUMENT NUMBER: 141:167823
TITLE: Selective mGlu5 antagonists for treatment of neuromuscular dysfunction of the lower urinary tract
INVENTOR(S): Leonardi, Amedeo; Testa, Rodolfo; Poggesi, Elena
PATENT ASSIGNEE(S): Recordati S.A., Switz.; Recordati Industria Chimica E Farmaceutica S.P.A.
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004067002	A2	20040812	WO 2004-EP951	20040130
WO 2004067002	A3	20041125		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
EP 1599204	A2	20051130	EP 2004-706676	20040130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006516587	T	20060706	JP 2006-501708	20040130

PRIORITY APPLN. INFO.: IT 2003-MI151 A 20030130
WO 2004-EP951 W 20040130

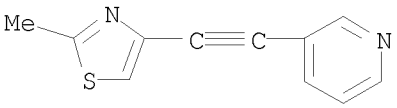
OTHER SOURCE(S): MARPAT 141:167823

AB Antagonists that are selective for the metabotropic mGlu5 receptor over at least one of the metabotropic mGlu1 receptor, mGlu2 receptor and mGlu3 receptor, and preferably selective over all three thereof, are useful for the preparation of medicaments for the treatment of neuromuscular dysfunction of the lower urinary tract in mammals. A wide variety of suitable compds. is described. The medicament may contain the selective mGlu5 antagonist as the sole active agent, or may also contain one or more addnl. therapeutic agents for the treatment of neuromuscular dysfunction of the lower urinary tract in mammals. Also provided are methods of identifying selective mGlu5 antagonists that are useful for treating neuromuscular dysfunction of the lower urinary tract in mammals.

IT 329205-68-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Selective mGlu5 antagonists for treatment of neuromuscular dysfunction of the lower urinary tract)

RN 329205-68-7 CAPLUS

CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



L4 ANSWER 59 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:604070 CAPLUS
DOCUMENT NUMBER: 141:236331
TITLE: Anxiolytic-like effects of MTEP, a potent and selective mGlu5 receptor agonist does not involve GABAA signaling
AUTHOR(S): Klodzinska, Aleksandra; Tatarczynska, Ewa; Chojnacka-Wojcik, Ewa; Nowak, Gabriel; Cosford, Nicholas D. P.; Pilc, Andrzej
CORPORATE SOURCE: Institute of Pharmacology, Department of Neurobiology, Polish Academy of Sciences, Krakow, 31343, Pol.
SOURCE: Neuropharmacology (2004), 47(3), 342-350
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

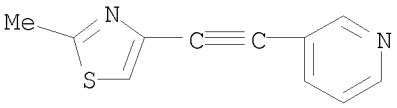
AB Several lines of evidence suggest a crucial involvement of glutamate in

the mechanism of action of anxiolytic drugs including the involvement of group I metabotropic glutamate (mGlu) receptors. Given the recent discovery of a selective and brain penetrable mGlu5 receptor antagonists, the effect of 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]-pyridine (MTEP), i.e. the most potent mGlu5 antagonist, was evaluated in established models of anxiety after single or repeated administration. We also studied if the anxiolytic effect of MTEP is mediated by mechanism involving the GABA-benzodiazepine (BZD) receptor complex. Expts. were performed on male Wistar rats or male Albino Swiss mice. The anxiolytic-like effects of MTEP were tested in the conflict drinking test and the elevated plus-maze test in rats as well as in the four-plate test in mice. MTEP (0.3-3.0 mg/kg) induced anxiolytic-like effects in the conflict drinking test (after single and repeated administration) and in the elevated plus-maze test in rats. In the four-plate test in mice, it exerted anxiolytic activity at a dose of 20 mg/kg. MTEP had no effect on the locomotor activity of animals. The anxiolytic-like effect of MTEP was not changed by BZD antagonist flumazenil. Moreover, a synergistic interaction between non-EDs of MTEP and diazepam was observed in the conflict drinking test. These data suggest that selective mGlu5 receptor antagonists mediated anxiolysis is not dependent on GABA-ergic system and that these agents may play a role in the therapy of anxiety.

IT 329205-68-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anxiolytic-like effects of MTEP does not involve GABAA signaling)

RN 329205-68-7 CAPLUS

CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 60 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:523298 CAPLUS

DOCUMENT NUMBER: 141:133562

TITLE: 5-[(2-Methyl-1,3-thiazol-4-yl)ethynyl]-2,3'-bipyridine: a highly potent, orally active metabotropic glutamate subtype 5 (mGlu5) receptor antagonist with anxiolytic activity

AUTHOR(S): Roppe, Jeffrey R.; Wang, Bowei; Huang, Dehua; Tehrani, Lida; Kamenecka, Theodore; Schweiger, Edwin J.; Anderson, Jeffery J.; Brodkin, Jesse; Jiang, Xiaohui; Cramer, Merryl; Chung, Janice; Reyes-Manalo, Grace; Munoz, Benito; Cosford, Nicholas D. P.

CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, San Diego, CA, 92121, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(15), 3993-3996
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

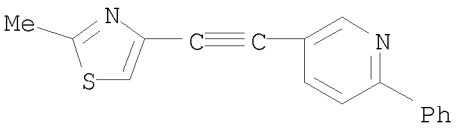
OTHER SOURCE(S): CASREACT 141:133562

AB Structure-activity relation studies leading to the discovery of a new,

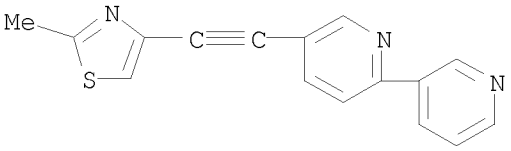
orally active mGlu5 receptor antagonist are described. The title compound, 5-[(2-methyl-1,3-thiazol-4-yl)ethynyl]-2,3'-bipyridine, is highly potent in vitro, has good in vivo receptor occupancy, and is efficacious in the rat fear-potentiated startle model of anxiety following oral dosing.

IT 329204-16-2P 329204-25-3P 329204-27-5P
329205-68-7P 722453-33-0P 727428-75-3P
727428-76-4P 727428-77-5P 727428-78-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and structure activity relations of [(methylthiazolyl)ethynyl]bipyridines as potent, orally active metabotropic glutamate subtype 5 receptor antagonist with anxiolytic activity)

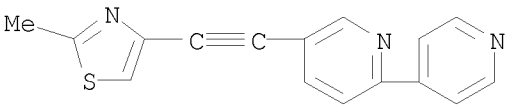
RN 329204-16-2 CAPLUS
CN Pyridine, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-phenyl- (CA INDEX NAME)



RN 329204-25-3 CAPLUS
CN 2,3'-Bipyridine, 5-[(2-methyl-4-thiazolyl)ethynyl]- (9CI) (CA INDEX NAME)



RN 329204-27-5 CAPLUS
CN 2,4'-Bipyridine, 5-[(2-methyl-4-thiazolyl)ethynyl]- (9CI) (CA INDEX NAME)



RN 329205-68-7 CAPLUS
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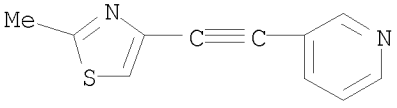

RN 722453-33-0 CAPLUS
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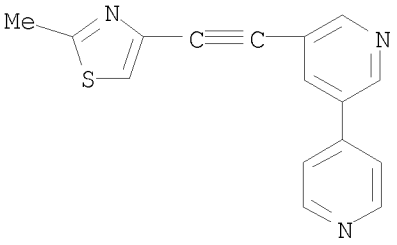
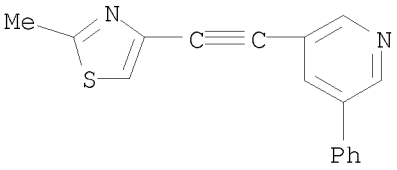
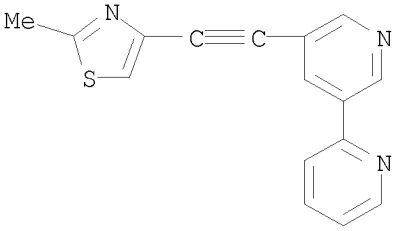


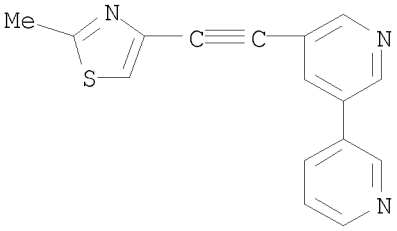
RN 727428-75-3 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]-5-phenyl- (CA INDEX NAME)



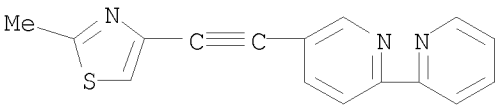
RN 727428-76-4 CAPLUS
CN 2,3'-Bipyridine, 5'-[(2-methyl-4-thiazolyl)ethynyl]- (9CI) (CA INDEX NAME)



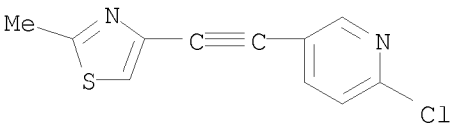
RN 727428-77-5 CAPLUS
CN 3,3'-Bipyridine, 5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



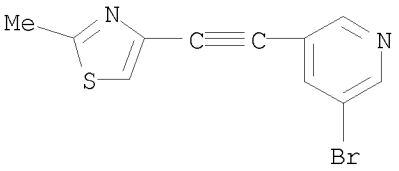
RN 727428-78-6 CAPLUS
CN 2,2'-Bipyridine, 5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



IT 329204-13-9P 329204-97-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and structure activity relations of [(methylthiazolyl)ethynyl]bipyridines as potent, orally active metabotropic glutamate subtype 5 receptor antagonist with anxiolytic activity)
RN 329204-13-9 CAPLUS
CN Pyridine, 2-chloro-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



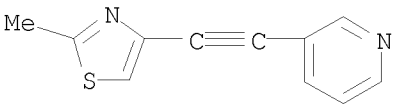
RN 329204-97-9 CAPLUS
CN Pyridine, 3-bromo-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



L4 ANSWER 61 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:486983 CAPLUS
DOCUMENT NUMBER: 141:235688
TITLE: Inhibition of human hepatic CYP isoforms by mGluR5 antagonists
AUTHOR(S): Green, Mitchell D.; Jiang, Xiaohui; King, Christopher D.
CORPORATE SOURCE: Merck Research Laboratories San Diego, San Diego, CA, 92121, USA
SOURCE: Life Sciences (2004), 75(8), 947-953
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Characterization of new chemical entities for their potential to produce drug-drug interactions is an important aspect of early drug discovery screening. In the present study, the potential for three metabotropic glutamate receptor antagonists to interact with recombinant human CYPs was investigated. 2-Methyl-6-(phenylethenyl)pyridine (SIB-1893), 2-methyl-6-(phenylethynyl) pyridine (MPEP) and 3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (MTEP) were moderate competitive inhibitors of recombinant human CYP1A2 (Ki, 0.5-1 μM). SIB-1893, but not MPEP or

MTEP, was also a moderate competitive inhibitor of CYP1B1. MPEP and MTEP were weak inhibitors of CYP2C19. None of the three compds. tested were significant inhibitors (IC50 values >50 μM) of CYP3A4, 2C9, 2D6, 2A6, 2B6 or 2E1. The results suggest that MTEP is a selective inhibitor of CYP1A2 and may prove to be a useful tool in studying drug-drug interactions involving this enzyme.

IT 329205-68-7, MTEP
RL: PAC (Pharmacological activity); BIOL (Biological study)
(inhibition of human hepatic CYP isoforms by mGluR5 antagonists)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

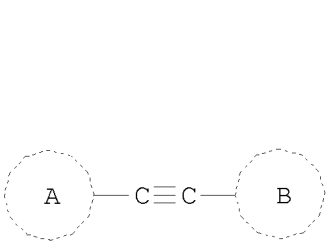


REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 62 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:371151 CAPLUS
DOCUMENT NUMBER: 140:391275
TITLE: Preparation of isotopically labeled heterocyclic alkyne derivatives as tracers for metabotropic glutamate receptor binding
INVENTOR(S): Cosford, Nicholas David Peter; Govek, Steven Patrick; Hamill, Terence Gerard; Kamenecka, Theodore; Roppe, Jeffrey Roger; Seiders, Thomas Jonathan
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004038374	A2	20040506	WO 2003-US33613	20031024
WO 2004038374	A3	20041028		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2503245	A1	20040506	CA 2003-2503245	20031024
AU 2003285957	A1	20040513	AU 2003-285957	20031024
EP 1556142	A2	20050727	EP 2003-779188	20031024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006513996	T	20060427	JP 2004-547079	20031024
US 20070060618	A1	20070315	US 2005-532634	20050425

PRIORITY APPLN. INFO.: US 2002-420809P P 20021024
WO 2003-US33613 W 20031024
OTHER SOURCE(S): MARPAT 140:391275
GI



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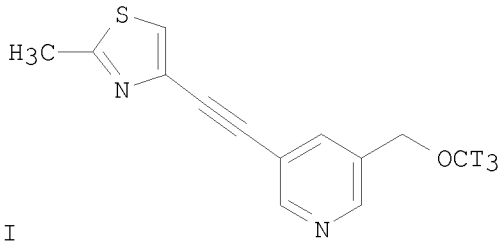
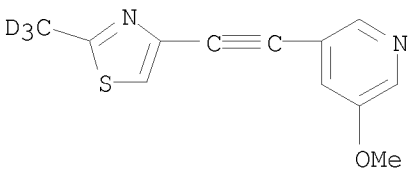


II

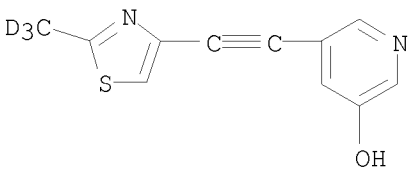
AB The present invention is directed to isotopically labeled alkyne derivative compds. I (A = optionally substituted heterocycle; B = optionally substituted aryl, heterocycle, C3-20 cycloalkyl, C3-20 cycloalkyneyl, C3-20 cycloalkadienyl, C3-20 cycloalkatrienyl, C3-2- cycloalkynyl, C3-20 cycloalkadiynyl; except when A = 6-methyl-2-pyridyl then B cannot = 3-MeOC6H4 or Ph) wherein the compound is isotopically labeled with at least one 11C, 13C,14C, 18F, 15O, 13N, 35S, 2H, or 3H atom. In particular, the present invention is directed to 11C, 13C, 14C, 18F, 15O, 13N, 35S, 2H, and 3H labeled heterocyclic alkynes and methods of their preparation The present invention further includes a method of use of the 11C, 18F, 15O, or 13N labeled heterocyclic alkyne compds. as tracers in positron emission tomog. (PET) imaging, particularly in the study of metabolic conditions in mammals, specifically conditions modulated by metabotropic glutamate receptors subtype 5 (mGluR5). Thus, Pd-catalyzed coupling of (5-bromopyridin-3-yl)methanol (preparation given) with 2-methyl-4-(trimethylsilylethynyl)-1,3-thiazole, followed by methylation with 11CH3I gave tritiated hetercyclic alkyne II. II was tested for in vitro binding of mGlu5 receptor protein.

IT 686767-95-3P 686768-37-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of isotopically labeled heterocyclic alkyne derivs. as tracers for metabotropic glutamate receptor binding)

RN 686767-95-3 CAPLUS
CN Pyridine, 3-methoxy-5-[[2-(methyl-d3)-4-thiazolyl]ethynyl]- (9CI) (CA INDEX NAME)

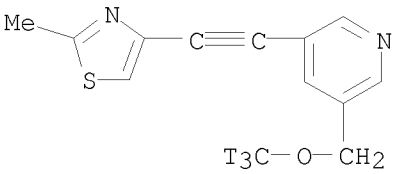


RN 686768-37-6 CAPLUS
CN 3-Pyridinol, 5-[[2-(methyl-d3)-4-thiazolyl]ethynyl]- (9CI) (CA INDEX NAME)



IT 524924-79-6P 686767-96-4P 686767-97-5P
686768-02-5P 686768-04-7P 686768-06-9P
686768-10-5P 686768-13-8P 686768-19-4P
686768-29-6P 686768-30-9P 686768-31-0P
686768-35-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isotopically labeled heterocyclic alkyne derivs. as tracers for metabotropic glutamate receptor binding)

RN 524924-79-6 CAPLUS
CN Pyridine, 3-(methoxy-t3-methyl)-5-[(2-methyl-4-thiazolyl)ethynyl]- (9CI) (CA INDEX NAME)



RN 686767-96-4 CAPLUS
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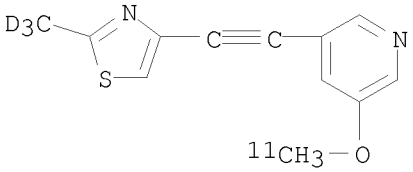
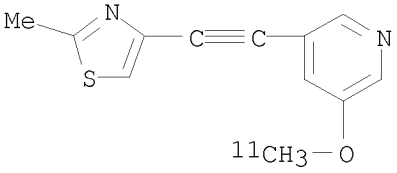
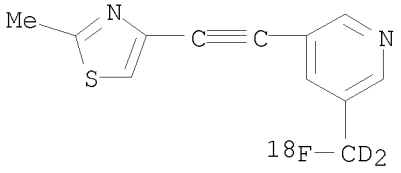


RN 686767-97-5 CAPLUS
CN Pyridine, 3-(methoxy-11C)-5-[(2-methyl-4-thiazolyl)ethynyl]- (9CI) (CA INDEX NAME)



RN 686768-02-5 CAPLUS

CN Pyridine, 3-(fluoro-18F-methyl-d2)-5-[(2-methyl-4-thiazolyl)ethynyl]- (9CI) (CA INDEX NAME)



RN 686768-04-7 CAPLUS
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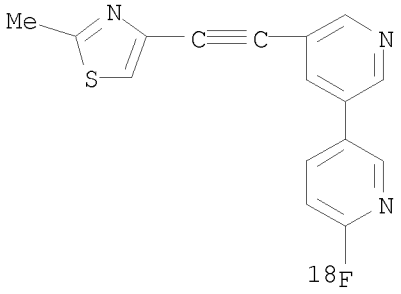
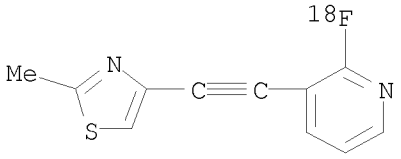


RN 686768-06-9 CAPLUS
CN Pyridine, 2-(fluoro-18F)-3-[(2-methyl-4-thiazolyl)ethynyl]- (9CI) (CA INDEX NAME)



RN 686768-10-5 CAPLUS
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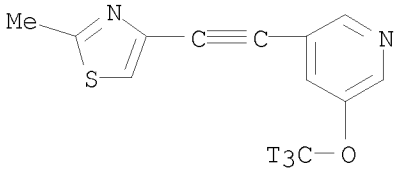
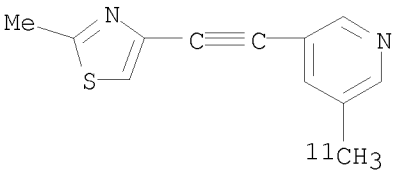
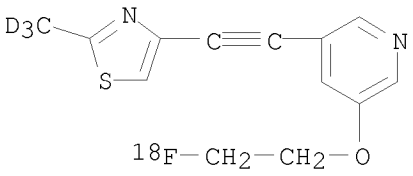


RN 686768-13-8 CAPLUS
CN Pyridine, 3-(methyl-11C)-5-[(2-methyl-4-thiazolyl)ethynyl]- (9CI) (CA INDEX NAME)



RN 686768-19-4 CAPLUS
CN Pyridine, 3-[2-(fluoro-18F)ethoxy]-5-[[2-(methyl-d3)-4-thiazolyl]ethynyl]-(9CI) (CA INDEX NAME)



RN 686768-29-6 CAPLUS
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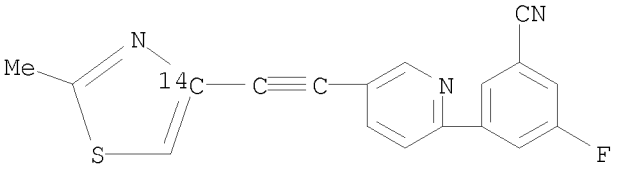
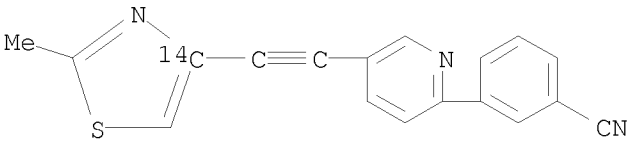
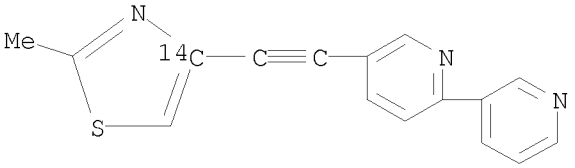


RN 686768-30-9 CAPLUS
CN Benzonitrile, 3-[5-[(2-methyl-4-thiazolyl-4-14C)ethynyl]-2-pyridinyl]-(9CI) (CA INDEX NAME)

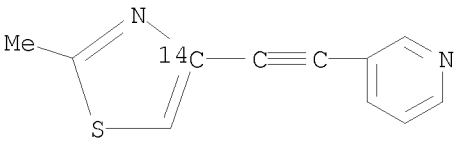


RN 686768-31-0 CAPLUS
CN 2,3'-Bipyridine, 5-[(2-methyl-4-thiazolyl-4-14C)ethynyl]- (9CI) (CA INDEX NAME)



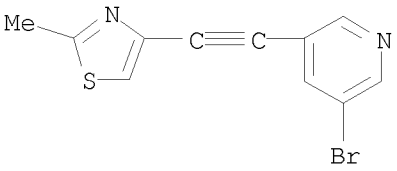
RN 686768-35-4 CAPLUS

CN Pyridine, 5-[(2-methyl-4-thiazolyl-4-14C)ethynyl]- (9CI) (CA INDEX NAME)

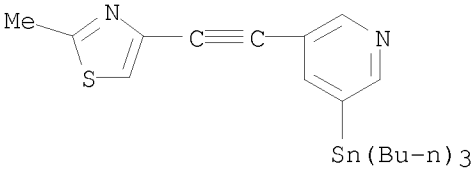


IT 329204-97-9 686768-41-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of isotopically labeled heterocyclic alkyne derivs. as tracers for metabotropic glutamate receptor binding)

RN 329204-97-9 CAPLUS
CN Pyridine, 3-bromo-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

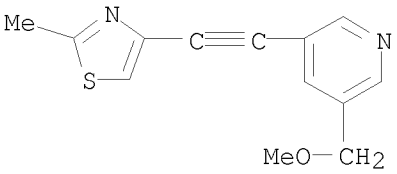


RN 686768-41-2 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]-5-(tributylstannyl)- (CA INDEX NAME)



IT 524924-75-2P 524924-81-0P 686768-48-9P
686768-49-0P 686768-56-9P 686768-57-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of isotopically labeled heterocyclic alkyne derivs. as tracers for metabotropic glutamate receptor binding)

RN 524924-75-2 CAPLUS
CN Pyridine, 3-(methoxymethyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 524924-81-0 CAPLUS
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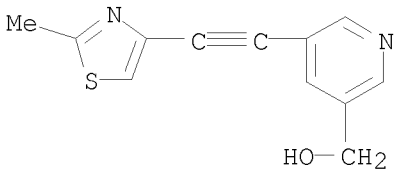
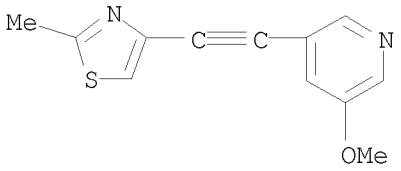


RN 686768-48-9 CAPLUS
CN Pyridine, 3-methoxy-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 686768-49-0 CAPLUS
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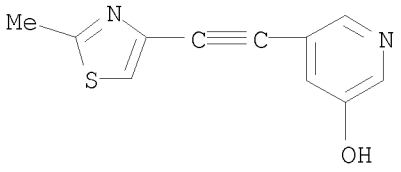

RN 686768-56-9 CAPLUS
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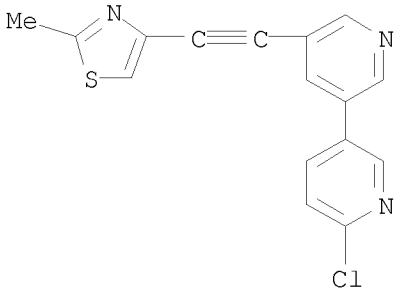
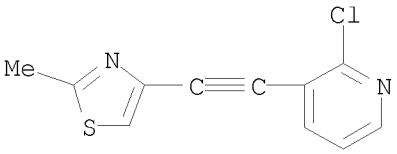


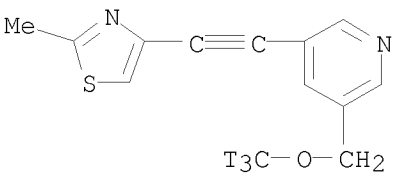
RN 686768-57-0 CAPLUS
CN Pyridine, 2-chloro-3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



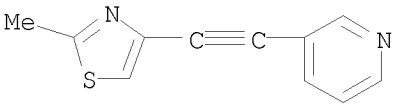
L4 ANSWER 63 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:91263 CAPLUS
DOCUMENT NUMBER: 138:379345
TITLE: [3H]-Methoxymethyl-MTEP and [3H]-Methoxy-PEPy: potent and selective radioligands for the metabotropic glutamate subtype 5 (mGlu5) receptor
AUTHOR(S): Cosford, Nicholas D. P.; Roppe, Jeffrey; Tehrani, Lida; Schweiger, Edwin J.; Seiders, T. Jon; Chaudary, Ashok; Rao, Sara; Varney, Mark A.
CORPORATE SOURCE: Department of Chemistry, Merck Research Laboratories, San Diego, CA, 92121, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(3), 351-354
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The design, synthesis, and characterization of two potent, non-competitive radioligands, [3H]-methoxymethyl-MTEP and [3H]-methoxy-PEPy, that are selective for the mGlu5 receptor are described.

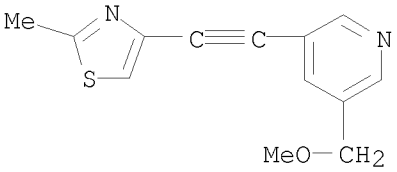
IT 524924-79-6P
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
([3H]-Methoxymethyl-MTEP and [3H]-Methoxy-PEPy in relation to design, synthesis and in-vitro characterization in rat brain membranes of potent and selective radioligands for metabotropic glutamate subtype-5 receptor)
RN 524924-79-6 CAPLUS
CN Pyridine, 3-(methoxy-t3-methyl)-5-[(2-methyl-4-thiazolyl)ethynyl]- (9CI) (CA INDEX NAME)



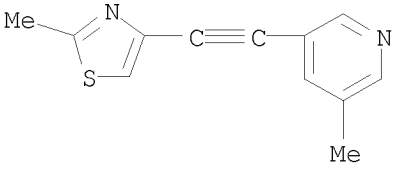
IT 329205-68-7P 524924-75-2P 524924-78-5P
RL: BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
([3H]-Methoxymethyl-MTEP and [3H]-Methoxy-PEPy in relation to design, synthesis and in-vitro characterization in rat brain membranes of potent and selective radioligands for metabotropic glutamate subtype-5 receptor)
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 524924-75-2 CAPLUS
CN Pyridine, 3-(methoxymethyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

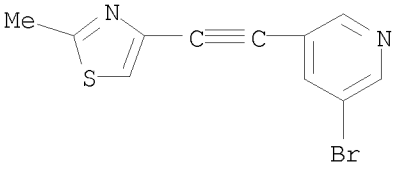


RN 524924-78-5 CAPLUS
CN Pyridine, 3-methyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

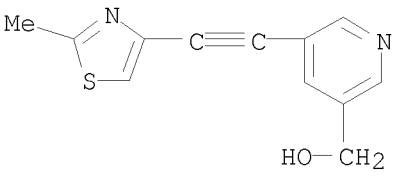


IT 329204-97-9P 524924-81-0P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
([3H]-Methoxymethyl-MTEP and [3H]-Methoxy-PEPy in relation to design, synthesis and in-vitro characterization in rat brain membranes of potent and selective radioligands for metabotropic glutamate subtype-5 receptor)

RN 329204-97-9 CAPLUS
CN Pyridine, 3-bromo-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

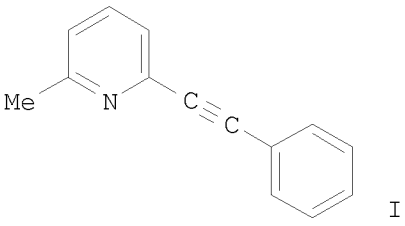


RN 524924-81-0 CAPLUS
CN 3-Pyridinemethanol, 5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

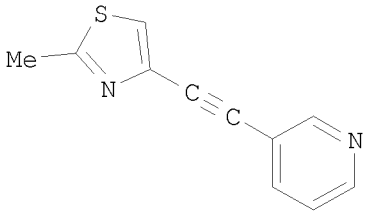


REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 64 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:943427 CAPLUS
DOCUMENT NUMBER: 138:170117
TITLE: 3-[(2-Methyl-1,3-thiazol-4-yl)ethynyl]- pyridine: A Potent and Highly Selective Metabotropic Glutamate Subtype 5 Receptor Antagonist with Anxiolytic Activity
AUTHOR(S): Cosford, Nicholas D. P.; Tehrani, Lida; Roppe, Jeffrey; Schweiger, Edwin; Smith, Nicholas D.; Anderson, Jeffrey; Bristow, Linda; Brodkin, Jesse; Jiang, Xiaohui; McDonald, Ian; Rao, Sara; Washburn, Mark; Varney, Mark A.
CORPORATE SOURCE: Merck Research Laboratories, San Diego, CA, 92121, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(2), 204-206
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:170117
GI



I

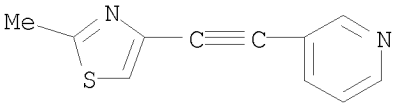


II

AB 2-Methyl-6-(phenylethynyl)pyridine (I), a potent noncompetitive mGlu5 receptor antagonist widely used to characterize the pharmacol. of mGlu5 receptors, suffers from a number of shortcomings as a therapeutic agent, including off-target activity and poor aqueous solubility Seeking to improve the properties of I led to the synthesis of compound II, a highly selective mGlu5 receptor antagonist that is 5-fold more potent than I in the rat fear-potentiated startle model of anxiety.

IT 329205-68-7P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, structure-activity relationship, and mGlu5 receptor antagonist activity of phenyl- and pyridinylethynylthiazoles via coupling reactions of halobenzene or halopyriidnes with Me[(trimethylsilyl)ethynyl]thiazole)
RN 329205-68-7 CAPLUS

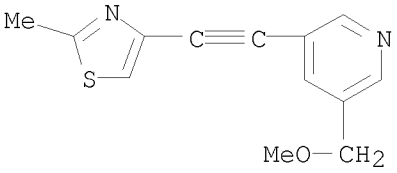
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 65 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:932568 CAPLUS
DOCUMENT NUMBER: 138:379544
TITLE: [3H]methoxymethyl-3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine binding to metabotropic glutamate receptor subtype 5 in rodent brain: in vitro and in vivo characterization
AUTHOR(S): Anderson, Jeffery J.; Rao, Sara P.; Rowe, Blake; Giracello, Darlene R.; Holtz, Greg; Chapman, Deborah F.; Tehrani, Lida; Bradbury, Margaret J.; Cosford, Nicholas D. P.; Varney, Mark A.
CORPORATE SOURCE: Department of Neuropharmacology, Merck Research Laboratories, San Diego, CA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 303(3), 1044-1051
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The binding of [3H]methoxymethyl-3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (methoxymethyl-MTEP), a potent and selective antagonist for metabotropic glutamate (mGlu)5 receptors, was characterized in rat brain both in vitro and in vivo. Non-specific binding, as defined with 10 μM 2-methyl-6-(phenylethynyl)-pyridine (MPEP), was less than 10% of total binding in rat brain membranes. The binding of [3H]methoxymethyl-MTEP was of high affinity (Kd = 20±2.7 nM), saturable (Bmax = 487±48 fmol/mg protein), and to a single site. The mGlu5 antagonists methoxymethyl-MTEP and MPEP displaced [3H]methoxymethyl-MTEP binding with IC50 values of 30 and 15 nM, resp. In vivo administration of [3H]methoxymethyl-MTEP (50 μCi/kg i.v.) revealed 12-fold higher binding in hippocampus (an area enriched in mGlu5 receptors) relative to cerebellum (an area with few mGlu5 receptors) in rats. Similarly, administration of [3H]methoxymethyl-MTEP to mGlu5-deficient mice demonstrated binding at background levels in forebrain, whereas wild-type littermates exhibited 17-fold higher binding in forebrain relative to cerebellum. Systemic administration of unlabeled mGlu5 antagonists methoxymethyl-MTEP and MPEP to rats reduced the binding of [3H]methoxymethyl-MTEP with ID50 values of 0.8 and 2 mg/kg i.p., resp., 1 h post-treatment. The mGlu5 agonist 2-chloro-5-hydroxyphenylglycine (CHPG) (0.3, 1, and 3 μmol) dose-dependently increased phosphoinositide (PI) hydrolysis in the hippocampus after i.c.v. administration in rats. CHPG-evoked increases in PI hydrolysis were blocked with MPEP at a dose (10 mg/kg i.p.) that markedly reduced [3H]methoxymethyl-MTEP binding in vivo. These results indicate that [3H]methoxymethyl-MTEP is a selective radioligand for labeling mGlu5 and is useful for studying the binding of mGlu5 receptors in rat brain in vitro and in vivo.
IT 528602-22-4

RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(methoxymethyl-MTEP binds to mGluR5 and is a useful tool for studying mGlu5 receptor function/signaling in rodent brain)
RN 528602-22-4 CAPLUS
CN Pyridine, 3-(methoxymethyl)-5-[(2-methyl-4-thiazolyl)ethynyl]-, labeled with tritium (9CI) (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 66 OF 66 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:167983 CAPLUS
DOCUMENT NUMBER: 134:222706
TITLE: Preparation of heterocyclic compounds as metabotropic glutamate receptor 5 (mGluR5) modulators
INVENTOR(S): Cosford, Nicholas D. P.; McDonald, Ian A.; Bleicher, Leo Solomon; Cube, Rowena V.; Schweiger, Edwin J.; Vernier, Jean-Michel; Hess, Stephen D.; Varney, Mark A.; Munoz, Benito
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016121	A1	20010308	WO 2000-US23923	20000831
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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CA 2383524	A1	20010308	CA 2000-2383524	20000831
EP 1214303	A1	20020619	EP 2000-957932	20000831
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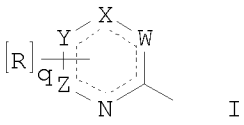
JP 2003508390	T	20030304	JP 2001-519688	20000831
AU 780009	B2	20050224	AU 2000-69482	20000831
PRIORITY APPLN. INFO.:			US 1999-387073 A2	19990831
			US 1999-387135 A2	19990831
			WO 2000-US23923 W	20000831

OTHER SOURCE(S): MARPAT 134:222706
GI

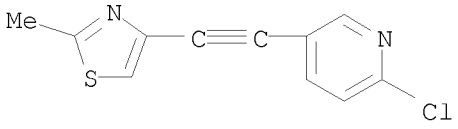


I

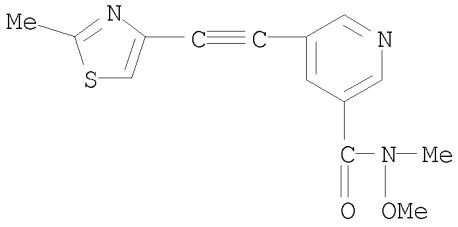
AB The title compds. I [ALB; A = 5-7 membered ring II (wherein at least one of W, X, Y and Z = (CR)p; p = 0-2, and the remainder of W, X, Y and Z = O, N, S; R = halo, (un)substituted aryl, heterocyclyl, etc.); L = (un)substituted alkenylene, alkynylene, azo; B = (un)substituted alkyl, cycloalkyl, heterocyclyl, etc.] and their pharmaceutically acceptable salts which are capable of modulating the activity of excitatory amino acid receptors such as metabotropic glutamate receptor, were prepared Thus, reacting 2-bromo-1,3-thiazole with phenylacetylene in the presence of CuI, Et3N and PdCl2(PPh3)2 in DME followed by treatment of the resulting 2-(phenylethynyl)-1,3-thiazole with p-TsOH afforded 2-(phenylethynyl)-1,3-thiazole, p-TsOH salt which showed IC50 of 0.1 nM - 10 μM in Ca+2 flux assay and analgesic efficacy in analgesic animal model (CFA model).

IT 329204-13-9P 329204-39-9P 329204-97-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

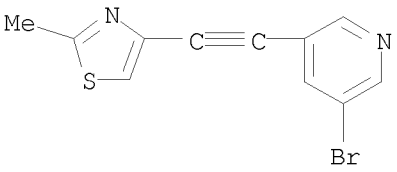
RN 329204-13-9 CAPLUS
CN Pyridine, 2-chloro-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 329204-39-9 CAPLUS
CN 3-Pyridinecarboxamide, N-methoxy-N-methyl-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

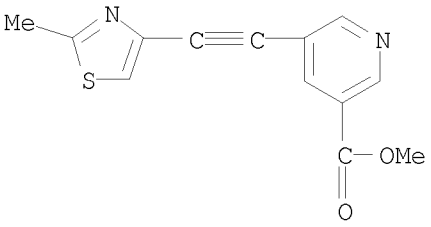


RN 329204-97-9 CAPLUS
CN Pyridine, 3-bromo-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)

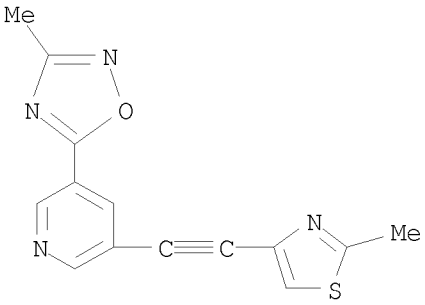


IT 329204-02-6P 329204-07-1P 329204-16-2P
329204-19-5P 329204-22-0P 329204-25-3P
329204-27-5P 329204-33-3P 329204-41-3P
329204-43-5P 329204-99-1P 329205-01-8P
329205-03-0P 329205-05-2P 329205-07-4P
329205-09-6P 329205-11-0P 329205-13-2P
329205-15-4P 329205-54-1P 329205-68-7P
329205-88-1P 329205-92-7P 329206-22-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

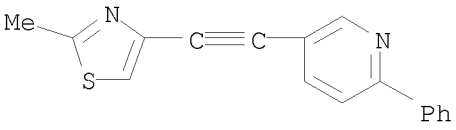
RN 329204-02-6 CAPLUS
CN 3-Pyridinecarboxylic acid, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-, methyl ester (CA INDEX NAME)



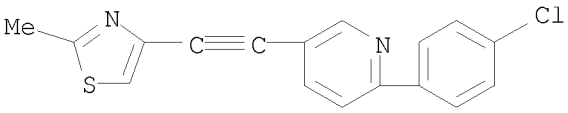
RN 329204-07-1 CAPLUS
CN Pyridine, 3-(3-methyl-1,2,4-oxadiazol-5-yl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



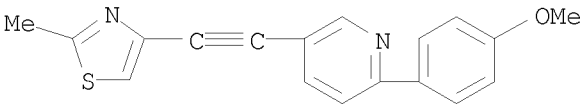
RN 329204-16-2 CAPLUS
CN Pyridine, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-2-phenyl- (CA INDEX NAME)



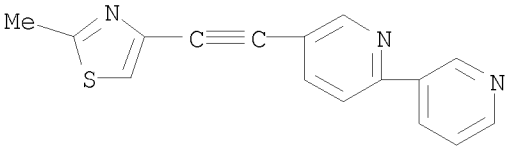
RN 329204-19-5 CAPLUS
CN Pyridine, 2-(4-chlorophenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



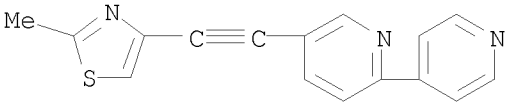
RN 329204-22-0 CAPLUS
CN Pyridine, 2-(4-methoxyphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



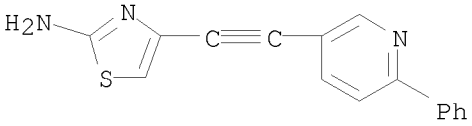
RN 329204-25-3 CAPLUS
CN 2,3'-Bipyridine, 5-[(2-methyl-4-thiazolyl)ethynyl]- (9CI) (CA INDEX NAME)



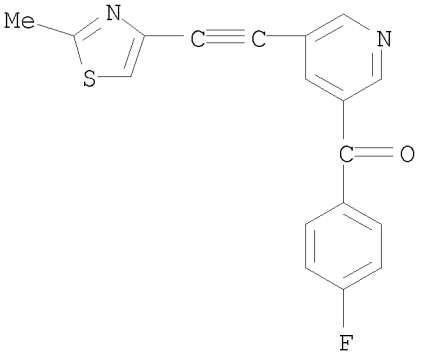
RN 329204-27-5 CAPLUS
CN 2,4'-Bipyridine, 5-[(2-methyl-4-thiazolyl)ethynyl]- (9CI) (CA INDEX NAME)



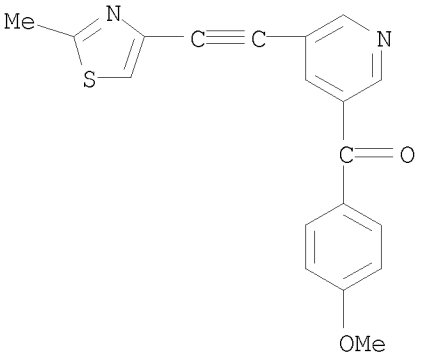
RN 329204-33-3 CAPLUS
CN 2-Thiazolamine, 4-[2-(6-phenyl-3-pyridinyl)ethynyl]- (CA INDEX NAME)



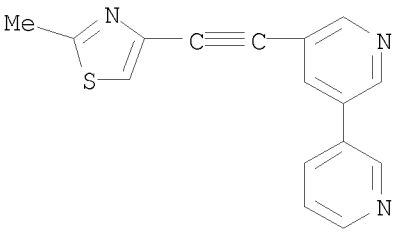
RN 329204-41-3 CAPLUS
CN Methanone, (4-fluorophenyl)[5-[2-(2-methyl-4-thiazolyl)ethynyl]-3-pyridinyl]- (CA INDEX NAME)



RN 329204-43-5 CAPLUS
CN Methanone, (4-methoxyphenyl)[5-[2-(2-methyl-4-thiazolyl)ethynyl]-3-pyridinyl]- (CA INDEX NAME)

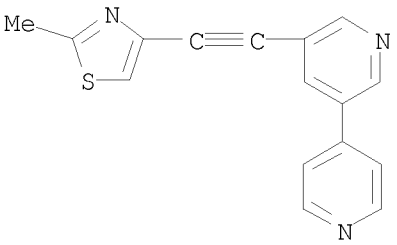


RN 329204-99-1 CAPLUS
CN 3,3'-Bipyridine, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:?) (CA INDEX NAME)



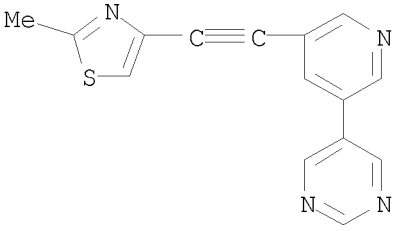
● x HCl

RN 329205-01-8 CAPLUS
CN 3,4'-Bipyridine, 5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:?) (CA INDEX NAME)



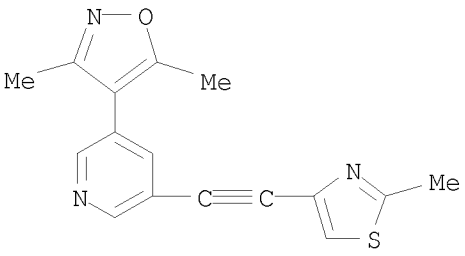
● x HCl

RN 329205-03-0 CAPLUS
CN Pyrimidine, 5-[5-[2-(2-methyl-4-thiazolyl)ethynyl]-3-pyridinyl]-, hydrochloride (1:?) (CA INDEX NAME)



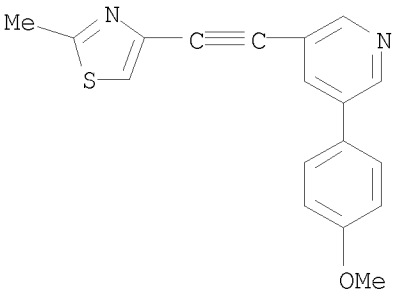
● x HCl

RN 329205-05-2 CAPLUS
CN Pyridine, 3-(3,5-dimethyl-4-isoxazolyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:?) (CA INDEX NAME)



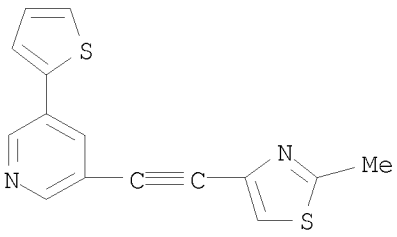
●x HCl

RN 329205-07-4 CAPLUS
CN Pyridine, 3-(4-methoxyphenyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]-, hydrochloride (1:?) (CA INDEX NAME)

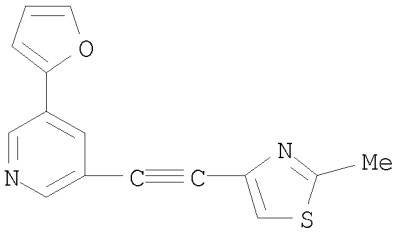


●x HCl

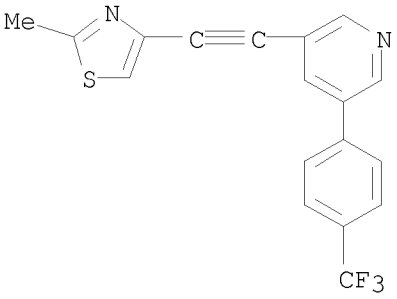
RN 329205-09-6 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]-5-(2-thienyl)- (CA INDEX NAME)



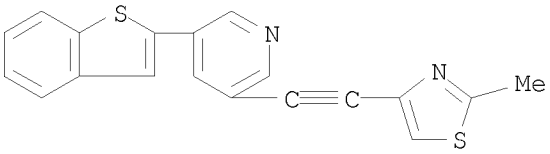
RN 329205-11-0 CAPLUS
CN Pyridine, 3-(2-furanyl)-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



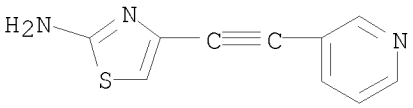
RN 329205-13-2 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]-5-[4-(trifluoromethyl)phenyl]- (CA INDEX NAME)



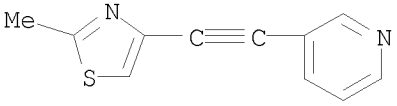
RN 329205-15-4 CAPLUS
CN Pyridine, 3-benzo[b]thien-2-yl-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



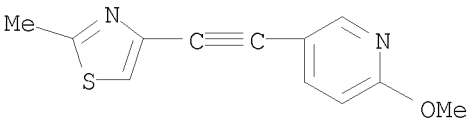
RN 329205-54-1 CAPLUS
CN 2-Thiazolamine, 4-[2-(3-pyridinyl)ethynyl]- (CA INDEX NAME)



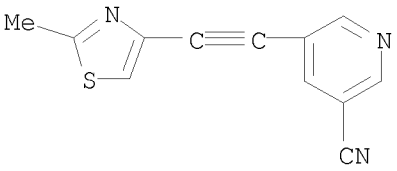
RN 329205-68-7 CAPLUS
CN Pyridine, 3-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



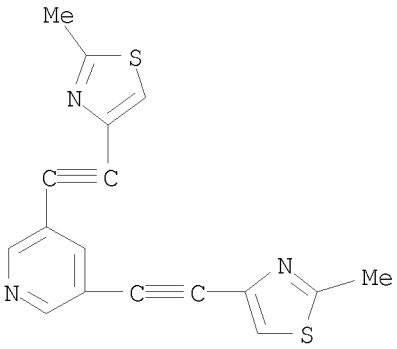
RN 329205-88-1 CAPLUS
CN Pyridine, 2-methoxy-5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 329205-92-7 CAPLUS
CN 3-Pyridinecarbonitrile, 5-[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



RN 329206-22-6 CAPLUS
CN Pyridine, 3,5-bis[2-(2-methyl-4-thiazolyl)ethynyl]- (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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